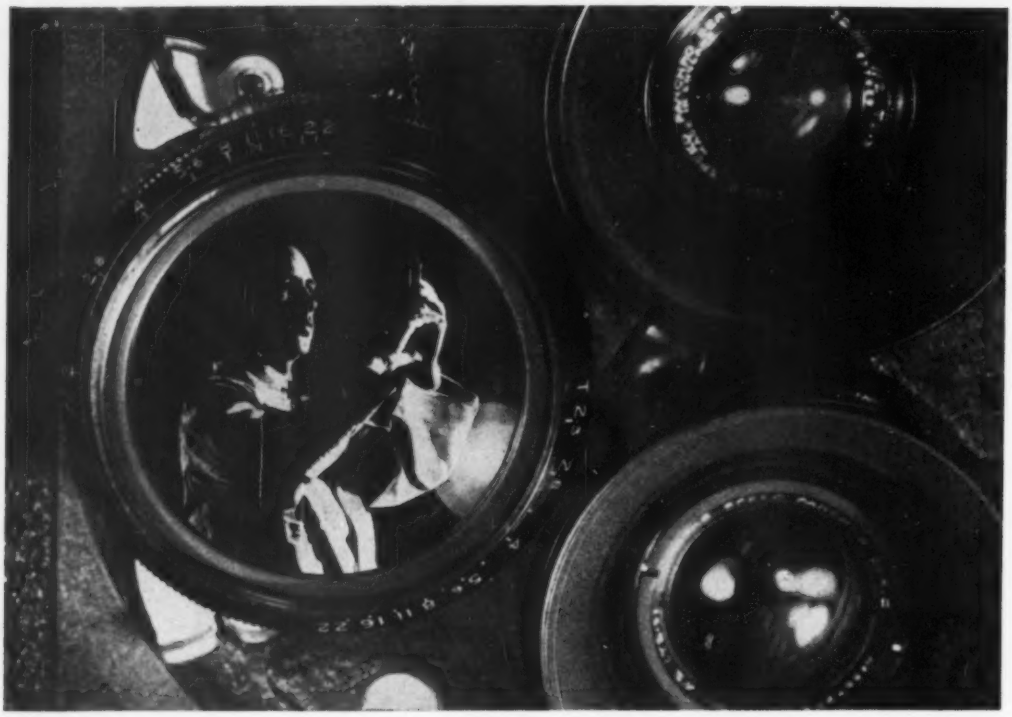
British Journal of Anaesthesia

JOINT EDITORS:
E. FALKNER HILL T. CECIL GRAY
Editor of Postgraduate Educational Numbers R. P. HARBORD

Volume XXXIII No. 8 August 1961

JOHN SHERRATT & SON : *Publishers*
ALTRINCHAM ENGLAND

I.C.I. MEDICAL FILMS



K25

I.C.I. has many films of value in teaching by demonstration and illustration, covering a wide range of medical and surgical procedures. A good example, recently added to the catalogue, is

PROSTATECTOMY UNDER 'FLUOTHANE'

Two operations of prostatectomy are shown, under identical conditions. One case received nitrous oxide, oxygen and scoline, the other 'Fluothane'. Measured blood losses in a series of cases by each method are given.

All the films are reputable aids in teaching, and are available free of charge to interested borrowers.
May we send you the 1961 I.C.I. Medical Film Catalogue?

Please send me a copy of the 1961 I.C.I. Medical Film Catalogue

NAME (BLOCK CAPITALS) .....

ADDRESS .....

These films are available for showing to medical audiences only.

I.C.I. FILM LIBRARY, IMPERIAL CHEMICAL HOUSE, MILLBANK, LONDON, S.W.1.

Medomin

Medomin adds to a positive hypnotic action a wide safety margin and freedom from after-effects, making it eminently suitable for patients of all ages.

Medomin presents the surety of hypnosis through the barbituric acid nucleus

Geigy

fresh awakening

Sound sleep

Dose: Adults 1 tablet, taken ½-1 hour before retiring. Children ¼-1 tablet, according to age.

Available in tablets of 200 mg Heptabarbitone (Cycloheptenylethyl barbituric acid)

Containers of 10, 100, 1000

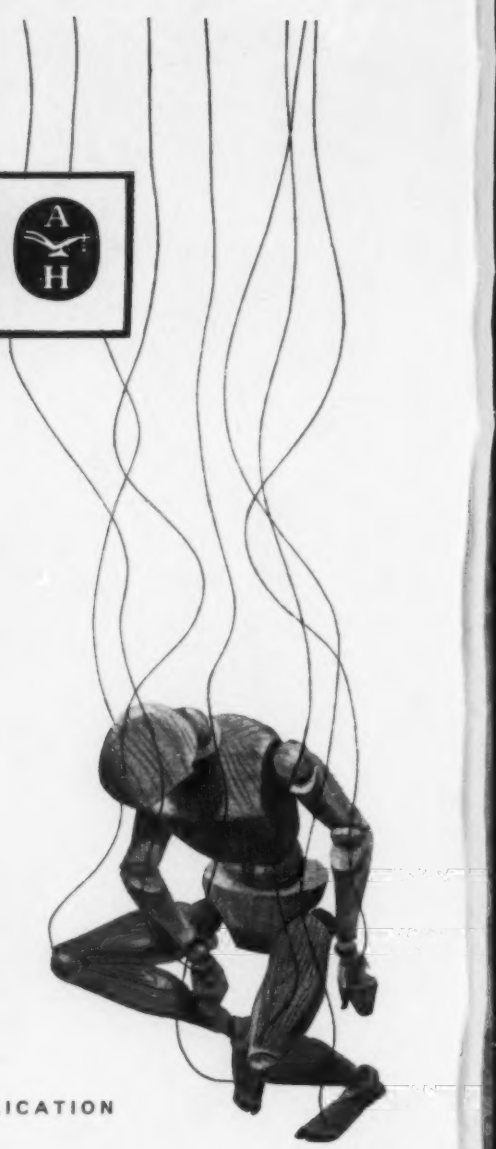
Geigy Pharmaceutical Company Ltd, Wythenshawe, Manchester 23.

PH 783

for deep but *controlled* relaxation

SCOLINE

- gives profound muscular relaxation for 2 to 6 minutes
- allows rapid return of spontaneous respiration and normal muscle tone, after use
- does not release histamine nor produce bronchospasm
- is free from toxic effects
- may be used with safety with all known anæsthetic agents
- reduces the risk of bone-fracture during E.C.T.



Scoline contains 50 mg. succinylcholine chloride in each c.c. Supplied in ampoules of 2 c.c. in boxes of 5 and 100 ampoules and in rubber-capped vials of 10 c.c.

STANDARD REFERENCE CARD ON APPLICATION

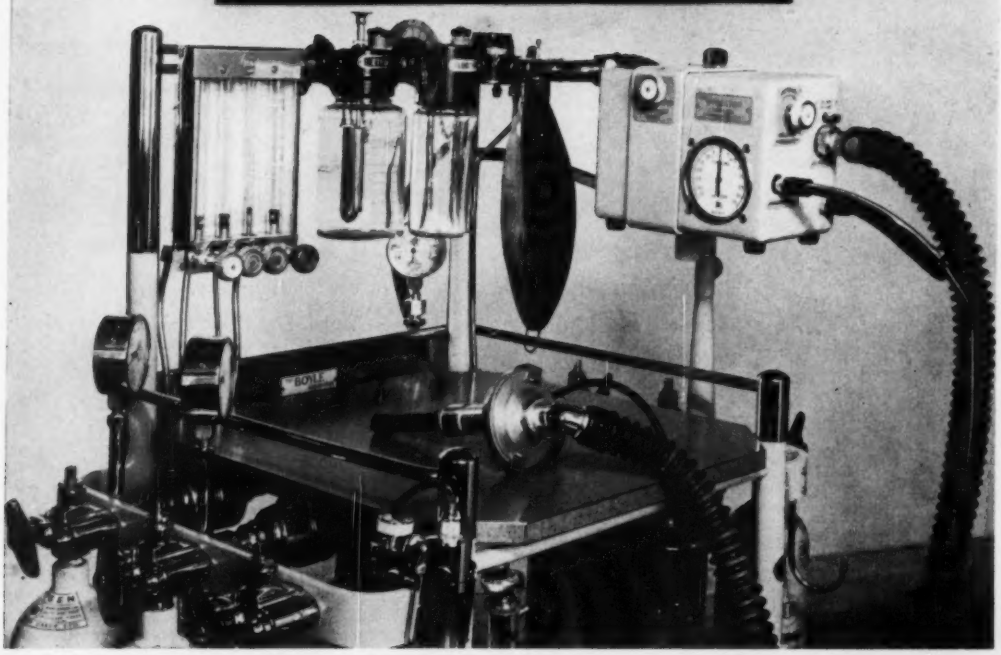
Manufactured in England by ALLEN & HANBURYS LIMITED LONDON E2

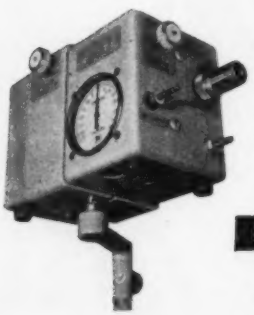
N58/515/H

BRITISH OXYGEN

equipment and gases used daily in the service of medicine

CYCLATOR Type P Mark 1





The CYCLATOR Type P Mark 1 is an intermittent positive pressure lung ventilator of the pressure cycling controller type. It is intended mainly for use on the open circuit of a Boyle type anaesthetic apparatus for automatic controlled respiration. Controls are provided permitting variation of lung inflation pressure up to 35 cms. H_2O, and expiratory time between $\frac{1}{2}$ second and 30 seconds.

FOR DETAILED INFORMATION PLEASE GET IN TOUCH WITH:

THE BRITISH OXYGEN COMPANY LTD

MEDICAL DEPARTMENT, SPENCER HOUSE, 27 ST. JAMES'S PLACE, LONDON S.W.1

NARPHEN

PAIN FREE BUT WIDE AWAKE...

Morphine-like analgesia
without narcosis — with NARPHEN

Narphen can supersede general anaesthetics in emergencies, minor surgery, orthopaedic procedures and obstetrics, when the full co-operation of the patient is needed. No elaborate pre-anaesthetic routine is necessary. Out-patients can be sent home and in-patients back to bed without lengthy post-operative observation.

Before, during and after general anaesthesia, Narphen controls pain efficiently and safely. It produces less respiratory depression than morphine or pethidine and does not cause hypotension. Narphen does not induce nausea or vomiting.

for deep analgesia without narcosis

Narphen is SNP brand Phenazocine (2'-hydroxy-5,9-dimethyl-2-phenethyl-6,7-benzomorphan hydrobromide)

Available in 1.1 ml. ampoules each containing 2 mg. phenazocine hydrobromide per ml. in aqueous solution. Boxes of 10 & 100 ampoules. Basic N.H.S. cost 15/- and 120/-. Exempt from Purchase Tax.

Subject to Dangerous Drugs Regulations.

SNP

Smith & Nephew *Pharmaceuticals* Limited
WELWYN GARDEN CITY · HERTFORDSHIRE

A wide choice of premedicants f

'PAMERGAN'
trade mark *brand*
PRE-ANAESTHETIC SOLUTIONS

Five carefully selected combinations of promethazine and pethidine with or without scopolamine or atropine.

'Pamergan' P100 Formula

Pethidine Hydrochloride B.P.	100 mg.
Promethazine Hydrochloride B.P.	50 mg.

in each 2 ml. ampoule

'Pamergan' P100/25 Formula

Pethidine Hydrochloride B.P.	100 mg.
Promethazine Hydrochloride B.P.	25 mg.

in each 1 ml. ampoule

'Pamergan' SP50 Formula

Scopolamine Hydrobromide B.P.	0·43 mg.
Pethidine Hydrochloride B.P.	50 mg.
Promethazine Hydrochloride B.P.	50 mg.

in each 2 ml. ampoule

'Pamergan' SP100 Formula

Scopolamine Hydrobromide B.P.	0·43 mg.
Pethidine Hydrochloride B.P.	100 mg.
Promethazine Hydrochloride B.P.	50 mg.

in each 2 ml. ampoule

'Pamergan' AP100/25 Formula

Atropine Sulphate B.P.	0·6 mg.
Pethidine Hydrochloride B.P.	100 mg.
Promethazine Hydrochloride B.P.	25 mg.

in each 1 ml. ampoule

HA8597

MANUFACTURED BY **MAY & BAKER LTD**

om the **M&B** range

'PHENERGAN'
trade mark brand
PROMETHAZINE HYDROCHLORIDE

Sedative, anti-emetic and anti-histaminic with a drying effect on secretions

'SONERGAN'
trade mark brand
PROMETHAZINE / BUTOBARBITONE

Sedative and hypnotic for use on the nights before and after operation.

'VALLERGAN'
trade mark brand
Forte Syrup
TRIMEPRAZINE TARTRATE

Specially designed for Children

Only a small volume of this pleasant tasting preparation is required

'Vallergan' is also presented as 2 ml. ampoules of a 2·5 per cent solution for injection and as suppositories of 50, 75 and 100 mg.

Detailed information is available on request

M&B brand Medical Products

DISTRIBUTORS: PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD · DAGENHAM

THE INTERNATIONAL MEDICAL ABSTRACTING SERVICE

EXCERPTA MEDICA

AMSTERDAM — LONDON — NEW YORK

offers to medical science:

For each medical specialty a MONTHLY ABSTRACTING JOURNAL containing abstracts in English from every available medical journal in the world.

Two special publications:

(1) SIDE EFFECTS OF DRUGS: an exhaustive and up-to-date review of the use of present-day drugs and their side effects, edited and compiled by L. Meyler, M.D.

(2) PHARMACOLOGICAL AND CHEMICAL SYNONYMS: a collection of more than 8,000 references from the medical literature of the world, compiled by E. E. J. Marler, M.D., M.Sc., Ph.D.

A TRANSLATION SERVICE for the rapid translation of medical publications and manuscripts.

LONDON OFFICE: *67 New Bond Street, W.1*

Telephone Mayfair 0329

CANADIAN ANÆSTHETISTS' SOCIETY JOURNAL

Editor

R. A. GORDON, C.D., B.SC., M.D., F.R.C.P.(C.), F.F.A.R.C.S.

Editorial Board

ALAN B. NOBLE, M.D., F.A.C.A. — E. A. GAIN, B.A., M.D.

LOUIS LAMOUREUX, M.D. — LEON LONGTIN, M.D., F.R.C.P.(C.)

★

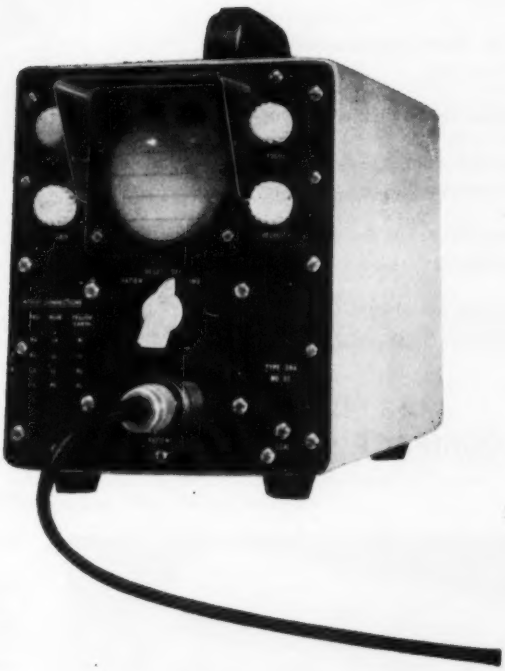
The Journal is issued quarterly for members of the Society and Subscribers. It contains original articles and reviews on clinical and basic science subjects related to Anæsthesia.

Annual Subscription $8.00 post paid

The Secretary
Canadian Anæsthetists Society
178 St. George Street, Toronto 5, Ontario, Canada

Presenting the

VIDEOGRAPH



Designed for routine monitoring of cardiac traces

Can be safely used in the presence of explosive anaesthetic gases

MEDICAL & INDUSTRIAL EQUIPMENT LTD.

SPECIALISTS IN ANAESTHETIC APPARATUS AND SURGICAL INSTRUMENTS

10 & 12 NEW CAVENDISH STREET, LONDON W.1

Telephone : WELbeck 1851 and 1504 Telegrams : NARCOSIS, LONDON

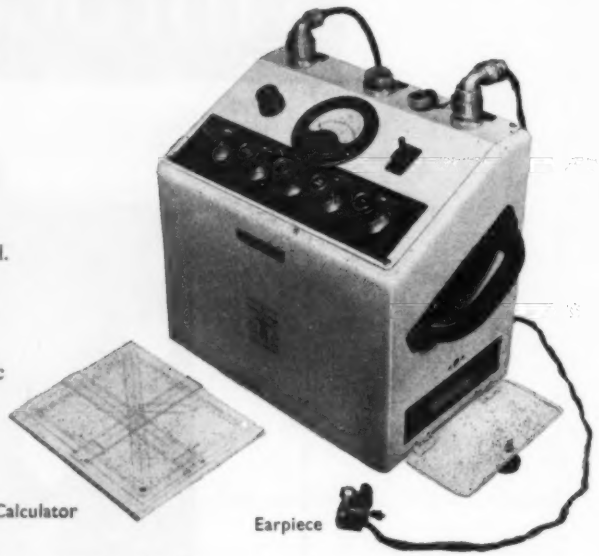
MANCHESTER: 152-154 Oxford Road
Phone : ARDwick 5906

TORONTO, CANADA: 132, St. Patrick Street
Phone : WALNUT 3-3845

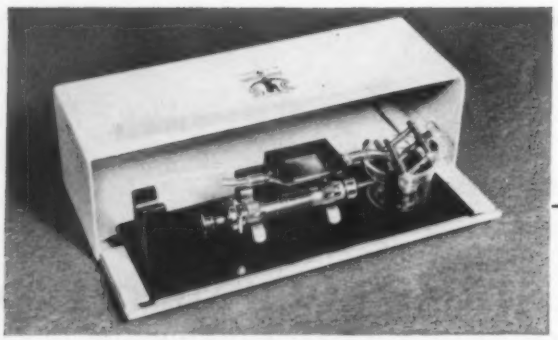
the STANLEY COX
OXIMETER model 'R'

For measurement of percentage blood oxygen saturation in vivo and in vitro.

- In vivo by photo-electric colorimetry of the intact ear.
- Established basic principals are followed.
- The practical aspects of oximetry are reduced to their simplest terms.
- An invaluable aid in the study of cardiac and respiratory functions.
- In vitro with use of cuvette attachments.



SAFE · COMPACT · ROBUST · PORTABLE



Throughout the procedure for taking percentage oxygen readings, all operational stages are positive and do not permit alternatives that can lead to error.

CUVETTE FOR WHOLE BLOOD OXIMETRY

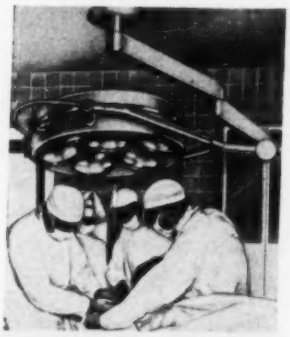
Please send for further details and prices to:-

STANLEY COX LIMITED (medical division)

Offices: ELLIS HOUSE · AINTREE ROAD · PERIVALE · MIDDLESEX
Telephone: ALPerton 1541

Showrooms: ELECTRIN HOUSE · 93/97 NEW CAVENDISH STREET · LONDON W.1

More light . . . less heat . . . with the NEW



'HANAULUX' OPERATING THEATRE LAMP

. . . *and* **easier manipulation without counterweight**

Two new models (Marks II and III) in the famous 'Hanaulux' range are now available. *Seven* reflectors give greater light intensity. Precision engineered suspension without counterweight ensures feather-light, finger-tip manipulation.

SIEREX LTD

Write or telephone for further details:

15-18 Clipstone Street London W.1 LANgham 2464

SUPPLIERS OF HANAULUX OPERATING LAMPS AND SIEMENS X-RAY EQUIPMENT

EDITORIAL EXECUTIVE COMMITTEE

General Editors

*E. FALKNER HILL, *Late Senior Anaesthetist, Manchester Royal Infirmary*

*T. CECIL GRAY, *Professor of Anaesthesia, University of Liverpool*

Editor of Postgraduate Educational Numbers

*R. P. HARBORD, *Reader in Anaesthetics, University of Leeds*

Consultant Editors

*M. H. ARMSTRONG DAVISON, *Consultant Anaesthetist, The United Newcastle upon Tyne Teaching Hospitals*

*J. W. DUNDEE, *Senior Lecturer in Anaesthetics, Queen's University of Belfast, Northern Ireland*

*W. W. MUSHIN, *Professor of Anaesthetics, Welsh National School of Medicine, Wales*

*J. F. NUNN, *Research Fellow, Royal College of Surgeons of England; Lecturer, University of London*

*H. H. PINKERTON, *Joint Lecturer in Anaesthetics, University of Glasgow, Scotland*

*R. F. WOOLMER, *Professor of Anaesthetics, Department of Anaesthesia, Royal College of Surgeons of England, London*

Assistant Editors

A. R. HUNTER, *Consultant Anaesthetist, Manchester Royal Infirmary*

J. E. RIDING, *Demonstrator in the Department of Anaesthesia, University of Liverpool*

Honorary Treasurer

*R. J. MINNITT, *Late Senior Honorary Anaesthetist, Royal Liverpool United Hospitals*

*In addition to those individuals on the EDITORIAL EXECUTIVE COMMITTEE whose names are marked with an asterisk, the following are members of the BOARD OF MANAGEMENT AND PROPRIETORS:

R. C. LAWRENCE, *Consultant Anaesthetist, United Leeds Hospitals*
T. J. C. MACDONALD, *Consultant Anaesthetist, Aberdeen Royal Infirmary*
A. G. MILLER, *Consultant Anaesthetist, Western Infirmary, Glasgow*
R. E. PLEASANCE, *Lecturer in Anaesthetics, University of Sheffield*
H. Q. O. WHEELER, *Consultant Anaesthetist, Department of Neurological Surgery, General Hospital, Sunderland*
W. D. WYLIE, *Consultant Anaesthetist, St. Thomas's Hospital, London*

Papers for publication and all editorial communications should be addressed to either of the Editors at 48–50 Bedford Street North, Liverpool, 7. Business communications should be addressed to the publishers: JOHN SHERRATT AND SON, Park Road, Altrincham, Cheshire. Published monthly. Annual subscriptions (post free): Inland £3 15*s.*; Overseas £4 4*s.*; United States and South Americas $12.00. © John Sherratt and Son, 1961.

'Fluothane' for patients of all ages

"A highly satisfactory, safe and predictable anaesthetic agent . . . " That was the conclusion of Abajian et al.* after experience with 'Fluothane' in over 5,000 entirely unselected cases. Their findings included a smooth induction, early suppression of pharyngeal and laryngeal reflexes, absence of secretions, adequate muscular relaxation and a rapid recovery.

* "Experience with Halothane ('Fluothane') in more than Five Thousand Cases." *J. Amer. Med. Ass.* (1959), **171**, 535.

Fluothane *–an I.C.I discovery*

Halothane B.P. Trade Mark

IMPERIAL CHEMICAL INDUSTRIES LIMITED PHARMACEUTICALS DIVISION WILMSLOW CHESHIRE

Ph 151

"I would have everie man write what he knowes and no more." —MONTAIGNE

BRITISH JOURNAL OF ANAESTHESIA

VOL. XXXIII, No. 8 AUGUST 1961

EDITORIAL

HEAD INJURY

Anaesthetists are becoming increasingly involved in the wise treatment of conditions previously considered to be in the surgeon's province—or even indeed within the range of a physician's duties. That this should be the case arises to a large extent from the notable part played by anaesthetists in Copenhagen during the very severe epidemic of poliomyelitis some ten years ago. The use of artificial ventilation after tracheostomy followed closely the methods used during many anaesthetic administrations and instituted a pattern which has happily not been forgotten.

Circumstances which may provoke such treatment range through poliomyelitis with bulbar paralysis, polyneuritis, tetanus under treatment with a total-paralysis regime, "stove-in chest", and chronic respiratory and cardiac failure. It is now becoming increasingly clear that tracheostomy is of value in many cases of severe head injury though respiratory aid may not be required.

The development of specialized neurosurgical units has to some extent resulted in a tendency to transfer all head injuries to these units. It is in fact not unknown to have such cases, urgently admitted to a general hospital, transferred immediately to such a unit without due regard being paid to their other and possibly more severe and deadly injuries. It is probably wiser to retain head injuries in the general hospital of their original admission until the whole situation has been properly assessed. Only a few head injuries need immediate craniotomy—and these usually need only control of continued bleeding, a procedure which can be done in most hospitals.

If early or immediate transfer is considered imperative, the advice of the anaesthetist should be sought on control of the airway, ventilation and management of secretions during the journey. There will be not a few occasions upon which the anaesthetist's clear duty will be to accompany such a patient in the ambulance and so ensure his arrival at the neurosurgical unit with good respiratory function

AN INDIAN GUEST

We in England can be justifiably proud of the part we have played in helping to develop anaesthesia in India by receiving the large number of Indian anaesthetists for postgraduate training in this country since the war. Neither should we forget the compliment paid to our standards of teaching and practice by those who have sought to learn from us. However, it is not enough to train the young specialist. We must also help to keep the senior man up to date by inviting him back again for personal contact in our centres. This we have so far largely failed to do but a start is now being made.

Through the liberal generosity of Messrs. May and Baker Ltd., the Faculty of Anaesthetists is able to sponsor a visit to Britain this summer of Dr. G. S. Ambardekar, Lecturer in Anaesthetics at the Seth G.S. Medical College and an Honorary Anaesthetist at the K.E.M. Hospital, Bombay. His anaesthetic training was obtained in the Nuffield Department of Anaesthetics in Oxford in 1946. He was elected a Fellow of our Faculty in 1954, President of the Indian Society of Anaesthetists in 1957, and he is now an examiner for the Diploma in Anaesthesia in the Medical Schools of Bombay, Hyderabad, Baroda and Nagpur.

We welcome Dr. Ambardekar to our shores once again and we can but hope that this excellent scheme is only a beginning and by one means or another will be regularly repeated.

Our thanks are due to Messrs. May and Baker for supporting this first experiment. Dr. Ambardekar will be able to renew old friendships and take back to India the latest ideas in the British anaesthetic field. His trip will be evidence of the continued interest of British anaesthetists in the work of their colleagues in India.

Brit. J. Anaesth. (1961), 33, 374

REBREATHING DURING CONTROLLED RESPIRATION WITH VARIOUS SEMICLOSED ANAESTHETIC SYSTEMS

BY

D. J. WATERS* AND W. W. MAPLESON
Department of Anaesthetics, Welsh National School of Medicine, Cardiff, Wales

THERE are two ways in which rebreathing can be avoided in anaesthetic systems. The first depends on the use of mechanical valves which deflect the expired gas so that it is lost from the system and cannot be re-inhaled. The second depends on the use of apparatus of such a design that the fresh-gas flow, if big enough, flushes out the expired gas before the next inspiration. A theoretical analysis (in which respiration was assumed to be spontaneous) predicted that rebreathing would be absent in the Magill attachment (system A) if the fresh-gas inflow was at least equal to the patient's minute-volume ventilation (Mapleson, 1954). The laboratory work of Woolmer and Lind (1954) and of Bracken and Sanderson (1955) and the theatre measurements of Davies, Verner and Bracken (1956) and of de Clive Lowe (1956) substantially agreed with this.

However, the Magill attachment is often used for controlled respiration. When this is done, the anaesthetist alters the apparatus by screwing down the expiratory valve so that, when the bag is squeezed, sufficient pressure can be built up in the system to inflate the lungs. This manoeuvre alters the behaviour of the system in that gas is now lost during the inspiratory phase, instead of during the expiratory phase. It cannot therefore be assumed that the conditions which guard against rebreathing during spontaneous respiration will do so during controlled respiration. This has been appreciated by Sykes (1959) who has published the results of an experimental investigation of rebreathing during controlled respiration with the Magill attachment. He demonstrated a substantial amount of rebreathing, even with a fresh-gas flow equal to the patient's minute-volume ventilation. There are, however, other semiclosed systems which, though inferior to the Magill attachment from the point of view of rebreathing for spontaneous respiration, are not necessarily inferior to it for controlled respiration. It appears worth while, therefore, to assess these other systems.

We have tried three approaches: qualitative theoretical analysis, quantitative mathematical analysis, and measurements on patients.

QUALITATIVE THEORETICAL ANALYSIS

Systems, A, B, C and D have been analyzed qualitatively, making the following simplifying assumptions:

(1) Plug flow of gases occurs in the corrugated tube and in the patient's airway (i.e. there is no longitudinal mixing of gases).

(2) The reservoir bag is not allowed to become taut during the expiratory phase (because this would impede expiration).

(3) At the end of inflation the pressure in the bag drops sharply to zero.

System A (*fig.* 1).

Consider the situation at the end of an inflation. The lungs are full and the bag is almost empty. The bag is then released and the lungs deflate. Gas flows from the lungs through the corrugated tube towards the bag. Provided that the bag is not allowed to become taut, the pressure in the system is low, and therefore no gas escapes through the valve during the expiratory phase. The whole of the expiration therefore resides in the tube at the end of the phase (fig. 1). If the tidal volume is large, some may even spill into the bag.

The bag is now squeezed, and immediately gas starts to flow into the lungs. Further, as soon as the pressure in the system rises above the opening pressure of the valve, gas begins to escape to the atmosphere as well as continuing to enter the lungs. At the start of the inflation, it is the stale

* Present address: University College, Ibadan, Nigeria

gas of the previous expiration in the tubing which is the first to approach X in figure 1. Some of this stale gas may thus be lost through the valve but some inevitably re-enters the patient. Towards the end of the inflation, when all the stale gas has been driven out of the tube, partly into the patient and partly out to the atmosphere, it is fresh gas from the supply line or bag which arrives at the point X. Some of this enters the patient but some is also inevitably lost through the valve. The system is thus seen to be inefficient when used for controlled respiration: some rebreathing is inevitable and some of the fresh gas is bound to be wasted.

System B (fig. 2).

Consider the process of deflation of the lungs. The bag is slack and the valve is closed, so gas flows from the lungs into the corrugated tube. The rate of flow is high at first but falls off as the lungs empty. At the same time there is a steady flow of fresh gas into the corrugated tube from the supply line. Just before the next inflation, therefore, there is a mixture lying in the tube whose composition may be represented diagrammatically as in figure 2, where the density of the dots in the corrugated tube indicates the concentration of alveolar gas.

Now the bag is squeezed. The plug of gas in the tube is shifted to the right. Some of it enters the patient and some is lost through the valve. It is divided up in a fashion which may be represented roughly by the broken line in figure 2: that portion below the broken line is destined for the patient, and that above is lost through the expiratory valve. At the same time, fresh gas enters from the supply line and goes direct to the patient.

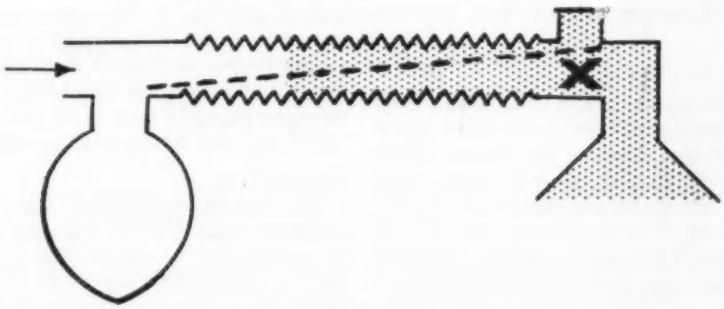


FIG. 1

System A (the Magill attachment) at the end of an expiration, according to the qualitative analysis. The dotted region indicates stale gas which has been expired, the clear region indicates fresh gas. Gas below the broken line is destined to go into the patient at the next inflation; gas above the line will go out through the valve. The arrow indicates the fresh-gas flow. X is a reference point (see text).

As the inspiratory phase progresses the pressure in the lungs rises and inflation becomes more and more difficult; the flow into the lungs tends to fall. On the other hand, the flow through the valve will, if anything, tend to increase during the course of the phase. Therefore, at the start of the phase, when there is stale gas at point X, most of this gas goes into the lungs. Conversely, towards the end of the phase, when fresh gas has reached the point X, most of it goes out through the valve. In figure 1 the gas below the broken line will enter the patient; that above the line will leave through the valve. In this system, therefore, the gases appear to be distributed in almost the worst fashion possible.

This system is better than system A on two counts. Firstly, as may be appreciated from the distribution of the dots and the position of the broken lines in figures 1 and 2, the portion of gas from the tube which enters the patient contains less alveolar gas with system B than with system

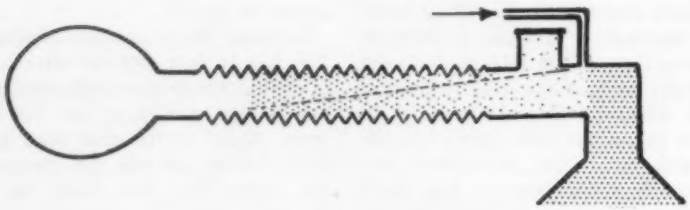


FIG. 2

System B at the end of an expiration. The density of the dots roughly indicates the concentration of alveolar gas. Gas below the broken line, together with fresh gas, indicated by the arrow, will enter the patient at the next inflation. At the same time gas above the broken line will be driven out through the valve.

A. Secondly, almost all the fresh gas that comes into system B during inflation goes into the patient.

System C (fig. 3).

This system can be derived from system B by omitting the corrugated tube. As in system B, the fresh gas still goes direct to the patient during inflation. But the alveolar and fresh gases, which travel to the left during expiration, now become mixed in the bag. Therefore, during inflation it is this mixture which goes out through the expiratory valve and which also, together with fresh gas from the supply line, enters the patient. This is in contrast to system B where the gas which was driven from the tube into the patient was relatively rich in fresh gas (fig. 2). Thus this system might be expected to be somewhat less efficient than system B, but still better than system A. The system shown in figure 4, in which the expiratory valve is replaced by a tap in the tail of the double-ended bag, may be expected to behave similarly.

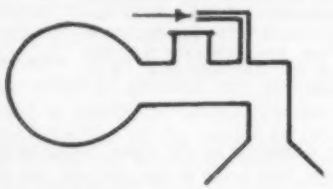


FIG. 3

System C.

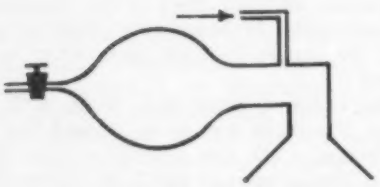


FIG. 4

An arrangement, with a double-ended bag and tap, which may be expected to behave similarly to system C.

System D (fig. 5).

This system differs from A, B and C in that the expiratory valve is remote from the patient. Fresh gas enters near the patient. The expiratory valve may be replaced by a tap on the tail of a double-ended bag (fig. 6) in which case the system becomes that recommended by Rees (1950) for paediatric use.

During expiration this system behaves in exactly the same way as system B and therefore, just before the start of an inflation, the situation will be as shown in figure 5, where the gas distribution towards the righthand end of the corrugated tube is the same as in figure 2.

During inflation, fresh gas goes directly to the patient, as in systems B and C, and the rest of the tidal volume is made up of gas from the corrugated tube. In this system, however, gas from the righthand end of the tube goes exclusively to the patient instead of being shared between the valve and the patient. In fact, all the gas to the right of the broken line in figure 5 will enter the patient. That to the left of the line will enter the bag during the next expiration and eventually find its way out through the expiratory valve.

For a given set of circumstances, the volume of gas which enters the lungs from the corrugated tube during inflation is the same for systems B

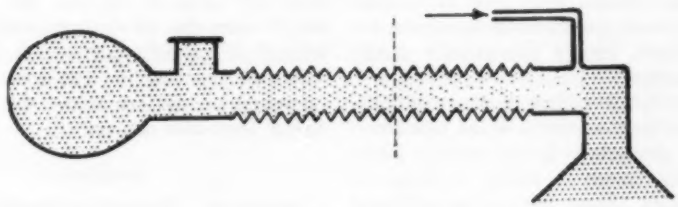


FIG. 5

System D at the end of an expiration. The density of the dots roughly indicates the concentration of alveolar gas. Gas to the right of the broken line, together with fresh gas, indicated by the arrow, will enter the patient at the next inflation.

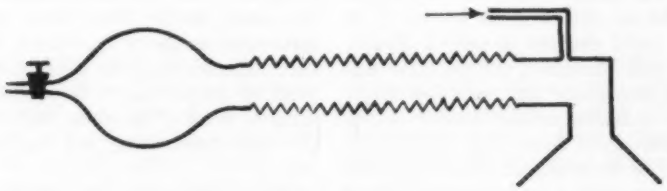


FIG. 6

An arrangement, with a double-ended bag and tap, as described by Rees for paediatric anaesthesia, which may be expected to behave similarly to system D.

and D, i.e. the volume to the right of the broken line in figure 5 is the same as the volume below the broken line in figure 2. It appears that less alveolar gas is contained in this volume in system D than is the case in system B. Hence it is to be expected that system D will be more efficient.

The order of merit would appear to be D, B, C, A.

MATHEMATICAL ANALYSIS

A mathematical analysis has been made of all four systems on the basis of the following assumptions:

(1) The system is in a steady state.
(2) The bag never becomes taut.
(3) The bag is squeezed according to a square wave of pressure.
(4) Plug flow occurs in the corrugated tubing and patient's airways.
(5) Complete mixing occurs in the reservoir bag.
(6) The resistance of the corrugated tube is negligible.
(7) The flow through the patient's airways is proportional to the pressure drop across them.

The order of merit arrived at in the qualitative analysis was verified for all likely conditions. The analysis also showed a very wide range of performance: system A appeared to involve a great deal of rebreathing and system D very little (see the second line of table II).

MEASUREMENTS ON PATIENTS

Six patients requiring controlled respiration for periods of more than 1 hour were studied in the operating theatre. They were intubated and the lungs were inflated manually 16 times per minute with a ratio of inspiratory time to expiratory time of about 1:3 and a tidal volume close to 500 ml, i.e. with the minute-volume ventilation close to 8 l./min. The total fresh-gas flow was 8 l./min (nitrous oxide 6 l./min and oxygen 2 l./min). The expired tidal volumes were monitored by a Wright ventilation meter. End-tidal carbon dioxide concentration was measured continuously by means of a Stanley Cox end-tidal sampler and carbon dioxide analyzer. The samples were withdrawn through a fine catheter inserted down the endotracheal tube. Readings were taken at 1-minute

intervals. Various systems were used in rotation on each patient, each system being connected for at least 12 minutes until a substantially steady reading was obtained.

A change in end-tidal carbon dioxide may indicate a change in the effectiveness of the ventilation or a change in the carbon dioxide output. There were no clinical reasons to expect a change in the carbon dioxide output but, as an additional check, system D, which was used at the start of all cases, was reverted to later, usually at the end of the case. So long as the end-tidal carbon dioxide was substantially the same each time that system D was used, it was assumed that the output had been the same for all systems used. In case 2, in addition to the rapid changes in carbon dioxide level associated with changes of system, there was a steady decline throughout the case. This might be attributed to a falling carbon dioxide output but it is more likely to be due to a gradual decline in the sensitivity of the analyzer. (The sensitivity was checked at the end of each case but not at the beginning; the zero was checked at intervals during each case.) This leads to some doubt over the absolute carbon dioxide concentrations in the different systems but to very little uncertainty over the relative concentrations.

Figure 7 shows how the carbon dioxide concentration varied in a typical case. The results of all the cases are summarized in table I. The amount of rebreathing in the different systems cannot be directly calculated but some indirect estimations have been made (see Appendix) and these are listed in the first line of table II. It will be seen that all systems involved a moderate amount of rebreathing, system A being the worst, but that, even so, the end-tidal carbon dioxide concentration did not exceed the normal physiological level with any system.

DISCUSSION

Comparison of the three approaches.

From table II it can be seen that the amount of rebreathing in system A according to the measurements on patients is much less than the theoretical value, while in system D it is much more. Altogether the differences between the systems are much smaller than those predicted by the mathematical theory or, indeed, than might have been expected from the qualitative analysis. However, the measurements do confirm the theoretical order of merit to the extent that system A involves the most rebreathing and that system C comes next.

There are two factors that may contribute to this discrepancy between theory and experiment. Firstly, the theoretical differences between systems are probably too high. Thus the last five assumptions made in the mathematical analysis were not strictly valid during the measurements and the conditions which then obtained deviated from the assumptions in such a way as to make the real differences between systems smaller than those predicted theoretically. Secondly, the experimental differences between systems may be too low. Thus when the alveolar ventilation is reduced,

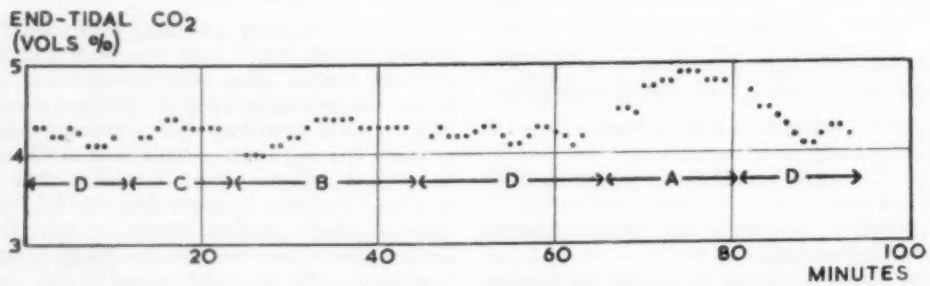


FIG. 7

End-tidal carbon dioxide concentration during manual controlled respiration (case No. 6). The letters indicate the systems used. With all systems, tidal volume ≃ 500 ml, rate = 16/min, fresh-gas flow = 8 l./min. Each point represents the average of three observations: that for the time against which the point is plotted and those for 1 minute before and 1 minute after.

TABLE I

End-tidal carbon dioxide in patients during controlled respiration with various semiclosed systems. In all cases: tidal volume ≃ 500 ml, rate = 16/min, fresh-gas flow = 8 l./min.

Patient	End-tidal carbon dioxide with system D (vols. %)	End-tidal carbon dioxide with other systems (expressed as a percentage of that found with system D)		
		A	B	C
1	3.9	117	—	—
2	4.4	127	—	—
3	3.8	112	100	—
4	5.1	121	100	—
5	3.8	—	92	103
6	4.2	117	102	102
Means	4.2	119	98	102

as when changing from system D to system A, the carbon dioxide output from the lungs is temporarily depressed and some of the carbon dioxide production of the body then accumulates in the tissues; the end-tidal carbon dioxide concentration then rises until the carbon dioxide output from the lungs is restored to the original level. In the measurements on patients the end-tidal carbon dioxide concentration seemed to stabilize within 12 minutes and in calculating the amounts of rebreathing shown in the first line of table II it was assumed that carbon dioxide output from the lungs was then back to the level obtaining before the alveolar ventilation was changed. However, according to the recent work of Farhi and Rahn (1960), the carbon dioxide output was probably still depressed after 12 minutes and would subsequently have increased very slowly, reaching the original level only after some hours. If this were so the values calculated for the alterations in alveolar ventilation on changing from one system to another would be too small and therefore the real differences between the systems would be greater than those shown in table II as derived from the measurements on patients.

TABLE II

Rebreathing in l./min during controlled respiration with the different semiclosed systems. Total ventilation = 8 l./min (500 ml. 16 times a minute), deadspace ventilation assumed to be 1.8 l./min.

	System			
	A	B	C	D
Estimate from measurements on patients	2.5	1.7	2.0	1.8
Estimate from mathematical theory	4.4	*	2.5	0.9

*A general solution could not be obtained for system B, but for those circumstances in which a solution could be obtained the amount of rebreathing was intermediate between that for C and that for D.

The magnitude of the errors in the theoretical values might be assessed by making more realistic assumptions; but then the mathematical equations, already complex, would become so cumbersome that they could only be solved on a large digital computer and the problem was not thought to be of sufficient importance to warrant this approach. However, an attempt has been made to assess the errors in the experimental values by programming a simple analogue computer, developed by one of us (W.W.M.) for other purposes, with the data of Farhi and Rahn, modified to suit the present conditions. This suggested that the end-tidal carbon dioxide with system A might increase from 119 per cent of that with system D observed experimentally after 15 minutes, to a final level of 135 per cent after some hours. This would increase the estimated difference in rebreathing between systems A and D from 0.7 l./min to 1.1 l./min.

In sum, therefore, it seems that the true amounts of rebreathing probably lie somewhere between the theoretical and experimental values given in table II. Nevertheless, the differences between the systems in terms of carbon dioxide levels shown in table I remain valid when the systems are used for 10 or 20 minutes, but they would probably become somewhat greater with prolonged usage.

Comparison with the results of Sykes.

Sykes (1959) gives values obtained from his laboratory model for the end-tidal carbon dioxide concentration during controlled respiration with system A under slightly different conditions from those used in the present work. If his results are corrected as far as possible to the present conditions (assuming that a 40-ml decrease in dead-space will result in a 40-ml increase in effective tidal volume in system A) it appears that an end-tidal carbon dioxide concentration of 4.9 per cent would have been expected in the present work if the fresh-gas flow had been 10 l./min. In fact a concentration of 5.1 per cent was found with a fresh-gas flow of 8 l./min. If the amount of re-breathing is not very sensitive to the fresh-gas flow in these circumstances the agreement would appear to be quite close.

However, Sykes also made measurements on three patients comparing spontaneous and controlled respiration in system A. The tidal volume and rate were the same with both types of respiration so that, since there should have been negligible rebreathing during the spontaneous respiration, the rise in end-tidal carbon dioxide on changing to controlled respiration provided a measure of the degree of rebreathing introduced. The rise in the first patient was roughly consistent with the present results but in the other two it was rather smaller than might have been expected. This might be due to the higher fresh-gas flow used by Sykes but, if so, the apparent agreement between the present work and his laboratory model experiments may be partly fortuitous.

Clinical implications.

In the present work none of the semiclosed systems studied was so inefficient as to lead to a high level of carbon dioxide when it was used with a fresh-gas flow and a minute-volume ventilation both equal to 8 l./min. Such a ventilation is rather higher than is commonly encountered in anaesthetized patients when respiration is spontaneous but it is less than that used by most anaesthetists whom we have observed carrying out controlled respiration. Therefore, there seems to be no reason to condemn any of the systems as totally unsuitable for controlled respiration. Nevertheless, the qualitative analysis suggests that system A is an illogical one to use for controlled respiration, and the measurements on patients show that this system does in fact give more rebreathing than the other systems. Therefore, if a semiclosed system is deemed advisable for any reason, system B or D, or possibly C, would seem more suitable.

Sykes (1959) has argued that the best approach is to use a non-rebreathing inflating valve, such as the Ruben (1955). This was done on two patients but in the process a defect of the valve was noticed: when the bag was squeezed, about 150 ml of fresh gas was lost through the expiratory valve before the bobbin completed its movement to the inflating position. Thus some of the 8 l./min of fresh gas was wasted and the patient's total ventilation was less than the fresh-gas flow. In fact the wastage of fresh gas with the Ruben valve was about equal to the amount of rebreathing with system D so that the alveolar ventilation and the end-tidal carbon dioxide concentration were about the same with both. However, the *total* ventilation with system D was higher than with the Ruben valve (the difference being the rebreathing) and therefore the mean intrathoracic pressure was higher with system D for the same effective ventilation. Since this is generally undesirable (Mushin, Rendell-Baker and Thompson, 1959) the Ruben valve does indeed have an advantage over system D. A similar effective ventilation might be achieved even with system A, without increasing the fresh-gas flow, if the total ventilation were increased sufficiently; but this would entail a still higher mean intrathoracic pressure.

CONCLUSIONS

It is perfectly possible to give adequate controlled respiration, with a fresh-gas flow of 8 l./min, with any of these four semiclosed anaesthetic systems. However, all the systems involve a certain amount of rebreathing, particularly system A, and they therefore entail a somewhat higher mean intrathoracic pressure, for a given effective ventilation, than would occur with a non-rebreathing inflating valve.

Therefore, if controlled respiration is to be performed without the use of soda lime, a non-rebreathing inflating valve would seem to be the most suitable apparatus, on the grounds that it gives a low mean intrathoracic pressure; but if these valves are rejected on other grounds—such as unreliability or inconvenience—systems B and

D, and possibly C, provide acceptable alternatives and are to be preferred to system A.

SUMMARY

Rebreathing in four semiclosed anaesthetic systems during controlled respiration, as distinct from spontaneous respiration, has been considered. The problem has been studied by both qualitative and quantitative theoretical analysis and by measurements on six patients. The three approaches agreed in finding systems B and D to involve the least rebreathing and system A the most, with system C intermediate, but the measurements on patients showed much smaller differences than the theoretical analysis predicted. With a tidal volume close to 500 ml, a rate of 16 respirations per minute and a fresh-gas flow of 8 l./min the end-tidal carbon dioxide concentration after about 15 minutes with system A was about one-fifth greater than with the other systems and did not exceed the normal physiological level. It is concluded that although a non-rebreathing inflating valve is to be preferred for performing controlled respiration in the absence of soda lime, systems B and D, and possibly C, form acceptable alternatives.

APPENDIX

ESTIMATION OF THE AMOUNT OF REBREATHING IN THE MEASUREMENTS ON PATIENTS

The amount of rebreathing with system D may be estimated on the basis of the following data.

(1) Total ventilation = alveolar ventilation + deadspace ventilation + rebreathed ventilation.

(2) Carbon dioxide output = alveolar ventilation × end-tidal carbon dioxide concentration.

(3) Nunn, Campbell and Peckett (1959) estimate the anatomical deadspace below the bottom of the endotracheal tube at 70 ml. The deadspace of the tube and connections may be put at 40 ml. Therefore the deadspace ventilation may be estimated at 110 ml × 16/min = 1.76 l./min. This is only a rough-and-ready estimate but in the present circumstances a 30 per cent error in the deadspace produces less than 0.1 l./min error in the estimated amount of rebreathing.

(4) It is assumed that there was no rebreathing with the Ruben valve. This seems fairly certain.

(5) It is assumed that the carbon dioxide output was the same in any given patient for all systems. (This assumption is commented upon in the main part of the paper.)

(6) It is assumed that for small changes in total ventilation in any one system the rebreathed ventilation is proportional to the total ventilation minus the deadspace ventilation. This is of somewhat doubtful validity: other possible assumptions give absolute values for rebreathing which deviate from those calculated here by up to ± 0.4 l./min, but the deviations in relative values are less than ±0.15 l./min.

Taking averages for the two cases in which the Ruben valve was used the following data are obtained: with the Ruben valve a total ventilation of 5.7 l./min gave an end-tidal carbon dioxide concentration of 4.05 per cent; with system D 7.5 l./min gave 3.9 per cent.

Therefore alveolar ventilation (Ruben valve), from (1) $=5.7-1.76=3.94$ l./min.

Therefore carbon dioxide output, from (2) $=3.94$ l./min $\times$ $4.05\%=159$ ml/min.

Therefore alveolar ventilation (system D), from (2) and (5) $=(159$ ml/min$)/3.9\%=4.09$ l./min.

Therefore rebreathed ventilation (system D) from (1) $=7.5-4.09-1.76=1.65$ l./min.

This is for a total ventilation of 7.5 l./min.

Therefore rebreathed ventilation (system D) for a total ventilation of 8 l./min, from (6)

$$=1.65\times\frac{8.0-1.76}{7.5-1.76}=1.79 \text{ l./min.}$$

The rebreathing with other systems has been similarly estimated by comparing each of them with system D. The total ventilations and end-tidal carbon dioxide concentrations were as follows. Average of 5 cases on which systems D and A were used: D, 7.7 l./min, 4.3 per cent; A, 7.7 l./min, 5.1 per cent. Average of four cases with systems D and B: D, 7.9 l./min, 4.2 per cent; B, 7.8 l./min, 4.2 per cent. Average of two cases with systems D and C: D, 7.95 l./min, 4.0 per cent; C, 8.05 l./min, 4.1 per cent. The results appear in the first line of table II.

ACKNOWLEDGMENTS

We are grateful to Professor William W. Mushin for his continual encouragement and advice throughout this work. Our thanks are also due to our surgical colleagues for their forbearance, and to Mr. E. K. Hillard, L.I.B.S.T., Senior Technician to this Department, for help with the measurements.

REFERENCES

Bracken, A., and Sanderson, D. M. (1955). Carbon dioxide concentrations found in various anaesthetic circuits. *Brit. J. Anaesth.*, **27**, 428.

Davies, R. M., Verner, I. R., and Bracken, A. (1956). Carbon dioxide elimination from semiclosed systems. *Brit. J. Anaesth.*, **28**, 196.

Farhi, L. E., and Rahn, H. (1960). Dynamics of changes in carbon dioxide stores. *Anesthesiology*, **21**, 604.

Lowe, S. G. de C. (1956). Discussion on carbon dioxide accumulations in anaesthetic circuits. *Proc. roy. Soc. Med.*, **49**, 220.

Mapleson, W. W. (1954). The elimination of rebreathing in various semiclosed anaesthetic systems. *Brit. J. Anaesth.*, **26**, 323.

Mushin, W. W., Rendell-Baker, L., and Thompson, P. W. (1959). *Automatic Ventilation of the Lungs*, p. 9. Oxford: Blackwell.

Nunn, J. F., Campbell, E. J. M., and Peckett, B. W. (1959). Anatomical subdivisions of the volume of respiratory dead space and effect of position of jaw. *J. appl. Physiol.*, **14**, 174.

Rees, G. J. (1950). Anaesthesia in the newborn. *Brit. med. J.*, **2**, 1419.

Ruben, H. (1955). A new non-rebreathing valve. *Anesthesiology*, **16**, 643.

Sykes, M. K. (1959). Rebreathing during controlled respiration with the Magill attachment. *Brit. J. Anaesth.*, **31**, 247.

Woolmer, R., and Lind, B. (1954). Rebreathing with a semiclosed system. *Brit. J. Anaesth.*, **26**, 316.

Brit. J. Anaesth. (1961), 33, 382

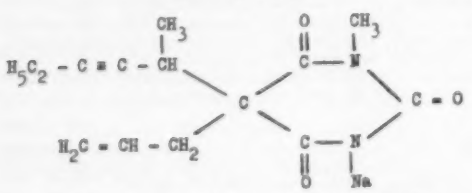
THE EFFECTS OF PREMEDICATION WITH PHENOTHIAZINE DERIVATIVES ON THE COURSE OF METHOHEXITONE ANAESTHESIA

BY

JOHN W. DUNDEE AND JAMES MOORE
Department of Anaesthetics, The Queen's University of Belfast, Northern Ireland

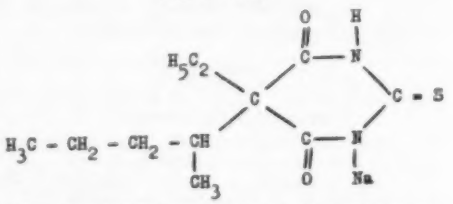
METHOHEXITONE is a rapidly acting barbiturate (fig. 1) which was originally described by Stoelting in 1957. Within the past year it has been subjected to clinical trials in this country and Jolly (1960) has verified the findings of Wyant and Chang (1959) and Wyant and Barr (1960) that recovery from methohexitone occurs more rapidly than from equivalent doses of thiopentone.

METHOHEXITONE



Sodium dl-1-methyl-5-(1-methyl-2-pentynyl) -5'-allyl-barbiturate

THIOPENTONE



Sodium, 5-ethyl-5' (1-methyl butyl) thiobarbiturate

FIG. 1
Formulae of methohexitone and thiopentone.

On reviewing the literature on methohexitone, Barron and Dundee (1961) found a lack of agreement concerning the incidence of complications associated with its use. This applied particularly to muscle twitchings and hiccough. Studies by the authors (Dundee and Moore, 1961a, b; Moore and Dundee, 1961a) suggest that the incidence of these complications is markedly affected by the nature of the premedication and that this may explain the discrepancies between the findings of various observers. Premedication with an analgesic drug (pethidine) was found to reduce significantly the incidence of spontaneous muscle movements as compared with the incidence after the use of atropine alone (Dundee and Moore, 1961a). On the other hand, when promethazine, which markedly increases sensitivity to pain (Moore and Dundee, 1961b, c), was given in premedication, the incidence of muscle twitchings after injection of a standard dose of methohexitone, rose to a prohibitively high level (Moore and Dundee, 1961a). This effect was also observed, but to a lesser degree, with hyoscine which also frequently causes an increase in sensitivity to somatic pain (Dundee and Moore, 1961b).

These observations have been made with premedicant drugs of different chemical composition and, despite the comparable conditions which applied to all the studies, it would seem unwise to draw too definite conclusions from the findings. Unknown interactions between methohexitone and the drugs used in premedication cannot be excluded. More valuable information would be obtained from the use of drugs of one chemical group, which vary only in their side chains and their analgesic activity.

Within the past year, the authors have been investigating the effects of various anaesthetic and premedicant drugs on sensitivity to somatic pain, using the method of analgesimetry described by Dundee and Moore (1960). The most recent

TABLE I

The phenothiazine derivatives used in this investigation.

Chemical group	Official name	Proprietary names	Dosage mg
Dimethyl amino propyl side chain	Chlorpromazine	Largactil Thorazine	25–50
	Promethazine	Phenergan	10 and 50
	Promazine	Sparine Verophen	25 and 100
	Trifluprom azine	Vespral Vesprin	20
	Trimeprazine	Vallergan	25
Piperazine side chain	Prochlorperazine	Stemetil Compazine	12.5
	Perphenazine	Fentazin Trilafon	5
	Trifluperazine	Stelazine	1
Piperidine side chain	Pecazine	Pacatal Lacumin	50

studies show that the phenothiazine derivatives cannot be considered as a homogenous group of drugs in respect to their effect on pain (Moore and Dundee, 1961c). The investigation included the nine phenothiazine derivatives which are listed in table I and their relative analgesic values are shown graphically in figure 2.

In the present investigation, the authors have studied the effects of premedication with the phenothiazine derivatives (in combination with atropine 0.6 mg) on the course of methohexitone anaesthesia, and have compared the results with those obtained using atropine alone and pethidine with atropine. An attempt has been made to correlate the findings with the chemical composition of the phenothiazine derivatives and with their analgesic action as shown in figure 2.

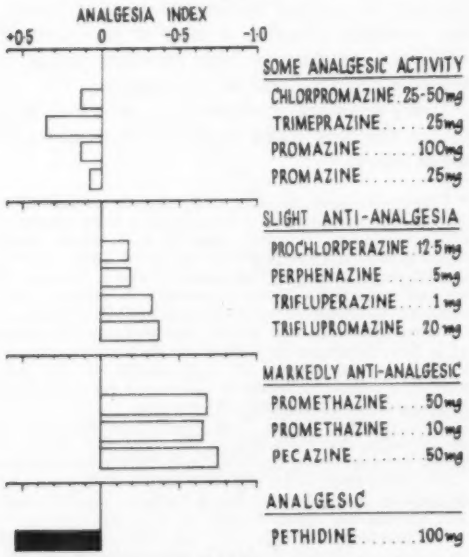


FIG. 2

Relative analgesic action of the nine phenothiazine derivatives, and pethidine, calculated acording to the method described by Moore and Dundee (1961c).

METHOD OF STUDY

A standard anaesthetic technique was employed for a standard operation throughout this investigation. Details of this have been described by Dundee and Moore (1961a) and are summarized below.

All patients were in good physical condition and underwent the operation of uterine curettage.

Anaesthesia was induced with 2 per cent methohexitone in a dosage of approximately 1.6 mg/kg. Anaesthesia was maintained using a mixture of 75 per cent nitrous oxide in oxygen with a total gas flow of 8 l./min. Intermittent doses of methohexitone were given to control reflex movement of the patient. Apart from occasions when suxamethonium was needed to control abnormal muscle movement, no other drugs were given. Pure oxygen was administered for exactly 1 minute at the end of the operation. All anaesthetics were administered personally by the authors.

Special charts were prepared which facilitated the recording of the following complications during anaesthesia.

1. Excitatory phenomena: tremor or spontaneous involuntary muscle movements.
2. Respiratory upset: cough, hiccough or laryngospasm.
3. Marked respiratory depression.
4. The degree and duration of hypotension following the induction dose. (Time permitted only the

recording of systolic blood pressure as estimated by palpation of the radial pulse.)
5. Induction and total dose of methohexitone.

Using the scheme described by Dundee and Riding (1960) each administration was graded as follows:
1. Uneventful
2. Slight upset, but not as marked as in grade 3.
3. Serious difficulties making surgery impossible or placing the patient's life in jeopardy (including severe, prolonged hypotension).

Two minutes after the end of the operation, the condition of each patient was classed as awake, safe (protective reflexes present) or unsafe (absence of protective reflexes).

Each patient was seen 1 hour after the end of anaesthesia and again at the end of 6 hours when the presence or absence of nausea and vomiting was noted.

Where possible, the anaesthetist was not aware of the nature of the premedication at the time of the administration.

Number of observations.

With the exceptions outlined below, the extent of the trial of each of the phenothiazine derivatives was determined by the method of sequential analysis described by Dundee and Moore (1961b). The basis of this is as follows:

Previous studies with methohexitone anaesthesia enabled the authors to establish the incidence of excitatory phenomena which was considered to be clinically acceptable, namely, that which was observed with atropine premedication (Dundee and Moore 1961a). Likewise, it was found that promethazine 50 mg increased the incidence of this complication to a prohibitive degree (Moore and Dundee, 1961a). From the findings of these two studies, a sequential plan was drawn (fig. 3) on which each consecutive case was plotted as showing the presence or absence of excitatory phenomena. This plan was constructed so that the effect of the premedicants under study on the incidence of excitatory phenomena could be classed as:

(*a*) Acceptable: atropine-like incidence.
(*b*) Unacceptable: promethazine-like incidence.
(*c*) Intermediate and probably worthy of further trial.

The maximum number of cases needed to reach a conclusion was 35.

As a further and more stringent test of the overall action of the phenothiazine derivative on the course of anaesthesia, a further plan was drawn. This was based on the incidence of grade 1 anaesthesia with atropine (acceptable) and promethazine 50 mg (unacceptable). This allowed the occurrence of hypotension and other undesirable effects which might be attributable to the pre-anaesthetic medication to be taken into account. As will be seen from figure 3, elimination of a compound by reason of its effect in increasing the incidence of excitatory phenomena following the injection of methohexitone automatically eliminates it by virtue of the low incidence of grade 1 anaesthesia. However, a compound may prove acceptable from the excitatory phenomena point of view and yet be eliminated because of a low incidence of grade 1 anaesthesia due to other causes.

The characteristics of the sequential plans are as follows:

	Incidence of excitatory phenomena	Incidence of grade 1 anaesthesia
h_1	+2.383	+3.635
h_2	−3.637	−2.383
s	0.553	0.447

$\alpha = 0.05$; $\beta = 0.10$

The reliability of these plans for use with data obtained at a date later than the control observations has been investigated by Dundee and Moore (1961b), and reasons for their preference to the more widely used "paired cases" technique of sequential analysis has been presented.

It was planned to use the phenothiazine derivatives in random order, making maximum use of "blind" ampoules early in the trial. Once a drug was rejected either on the basis of a high incidence of excitatory phenomena or a low incidence of grade 1 anaesthesia, it use was to be stopped. However, trials with a satisfactory compound continued until it was accepted by both the criteria set out above, or until it was administered as premedication to 35 patients. Thus, contrary to accepted British standards of justice, one rejection classified a drug as unacceptable while two acceptances were necessary before it was considered suitable for everyday use.

It was necessary, on occasions, to alter standards to suit the drug under study and the exceptions are as follows:

Chlorpromazine 50 mg. This was eliminated after only 9 administrations on account of a high incidence of hypotension. However, since it is a widely used drug, it was felt necessary to study its effect on the incidence of excitatory phenomena and a further 10 patients were given 25-mg doses until its action in this respect was shown to be similar to that of atropine.

Promazine 100 mg, while accepted on the basis of a low incidence of excitatory phenomena, caused a too marked degree of tachycardia in the preoperative period to justify its continued use. A further trial was carried out using a 25-mg dose.

Trimeprazine 25 mg. Two frightening episodes of hypotension occurring before the induction of anaesthesia terminated its use after only 10 administrations.

Prochlorperazine 25 mg. Postoperative hypotension limited its use to 8 cases but a further complete study was carried out using a dose of 12.5 mg.

Promethazine 10 mg. Although eliminated because of a low incidence of grade 1 anaesthesia after only 20 observations, it was desired to compare its effect on the incidence of excitatory phenomena with that of the 50-mg dose. The trial was therefore continued until a total of 36 observations had been made.

Pecazine 50 mg. Its early elimination on grades of anaesthesia after 8 administrations was due almost entirely to the incidence of excitatory phenomena. Because of the relationship which had been observed with other drugs between this incidence and "anti-analgesic" action, the trial was continued until the frequency of this side effect reached the incidence required to class it as "promethazine-like". This was considered justifiable since excitatory phenomena are not as dangerous from the patient's point of view as severe hypotension and abnormal muscle movements can be abolished with a small dose of suxamethonium.

The value of the sequential plan in making it possible to screen a large number of drugs with the minimum number of cases is demonstrated by the fact that in this trial nine phenothiazine derivatives were tested. In eight of these it was possible to come to a definite conclusion with a total of only 296 anaesthetics.

RESULTS

It would be impracticable to show the progress of the trial of each drug on the sequential plans in complete detail and the compromise arrangement depicted in figure 3 is presented, with table II for further guidance. Figure 3 shows the results obtained using chlorpromazine 25–50 mg in detail and shows the points at which the other drugs arrived at the limits of acceptance or rejection, or the final number of observations at which the trial was terminated. In order to demonstrate the superiority of pethidine as a premedication for use with methohexitone, and to verify previous findings on its beneficial effects on the course of anaesthesia, data from recent cases are also included in figure 3. It should be pointed out that the data for promethazine 50 mg included in this figure are those obtained in an earlier trial of this drug (Moore and Dundee, 1961a), since it was not felt justifiable to continue its use.

The order of listing the phenothiazine derivatives in table II is the same as that in table I and the relationship between the incidence of excitatory phenomena and the anti-analgesic action is apparent. This will be discussed in more detail later.

In order to validate further comparisons between different phenothiazine derivatives, it is

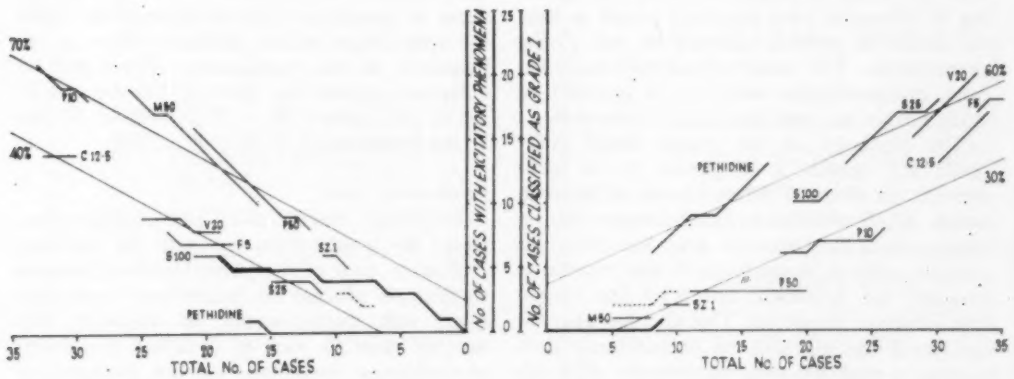


FIG. 3

Sequential plans showing the effect of chlorpromazine 25–50 mg on the course of methohexitone anaesthesia and the number of cases at which other phenothiazines were accepted or rejected from the trial according to the criteria outlined in the text. Similar data for pethidine 100 mg is included for comparison.

Thick continuous line = chlorpromazine 25–50 mg.

P	10	=	Promethazine 10 mg	F	5	=	Perphenazine 5 mg
P	50	=	Promethazine 50 mg	V	20	=	Triflupromazine 20 mg
M	50	=	Pecazine 50 mg	SZ	1	=	Trifluperazine 1 mg
S	25	=	Promazine 25 mg	C	12.5	=	Prochlorperazine 12.5 mg
S	100	=	Promazine 100 mg	- - - - - - -		=	Trimeprazine 25 mg (incomplete study).

TABLE II

Explanation of the results of figure 3.

Phenothiazine	Dose (mg)	No. of cases	Incidence of excitatory phenomena	Incidence of Grade 1 anaesthesia
Chlorpromazine	25–50	19	A	U
Promazine	100	22	A	—
Promazine	25	31	A	A
Trimeprazine	25	10	—	—
Prochlorperazine	12.5	34	A	O
Perphenazine	5	38	A	O
Trifluperazine	1	11	O	U
Triflupromazine	20	34	A	A
Promethazine	50	37	U	U
Promethazine	10	36	U	U
Pecazine	50	24	U	U

A = Incidence acceptable in clinical practice.
U = Unacceptable for clinical use.
O = No decision reached.
— = Trial not completed for reasons given in text.

necessary to establish that the observations were carried out on comparable groups of patients. The average age and weight of the patients, the mean duration of the anaesthesia and operative procedures and the average induction dose of methohexitone (mg/kg) in each of the series is shown in table III. For reasons which will be obvious later, the details of patients receiving 100 and 25 mg of promazine have also been pooled as have the details of patients receiving 50 and 10 mg promethazine. The scatter of induction doses has been calculated only where it is intended to study further the total barbiturate requirements.

The similarity of the groups under study (table III) enables a comparison to be made between the effects of different forms of premedication. All observations on blood pressure changes relate only to the induction dose. Since this was constant with all premedicants it was possible to compare the deleterious effects of the various phenothiazine derivatives. This also simplifies the analysis of the effects of the phenothiazine derivatives on methohexitone requirements. Although there are small variations in the average duration of anaesthesia and operation with the different drugs, these are of no significance since the total dose of methohexitone was invariably given during the first 5 minutes of the administration.

For clarity of presentation, the literature pertinent to each facet of the action of the selected phenothiazine derivatives on barbiturate narcosis will be discussed as near as possible to the relevant results.

Excitatory phenomena.

The percentage incidence of complications with each of the phenothiazine derivatives is shown in table IV, which also includes control data for atropine 0.6 mg and pethidine 100 mg combined with atropine 0.6 mg. Figure 3 shows that promethazine 10 mg and 50 mg and pecazine 50 mg each increased the incidence of excitatory phenomena in comparison with atropine alone, while the other drugs had no significant effect on the frequency of this complication. There was no difference between the effect of 100 mg and 25 mg of promazine ($0.50 > P > 0.40$) or 50 and 10 mg promethazine ($0.20 > P > 0.10$).

Respiratory upset.

Excluding trimeprazine and trifluperazine, where the numbers are too small for statistical evaluation, none of the phenothiazine derivatives significantly affected the incidence of respiratory upset with methohexitone, as compared with atropine alone. In view of the effect of different phenothiazine derivatives on the incidence of excitatory phenomena, it may be of some importance to record that the difference between the incidence of respiratory complications with atropine and the phenothiazine derivatives more nearly reached accepted levels of significance with promethazine 50 and 10 mg and pecazine 50 mg ($0.10 > P > 0.05$) than with any of the other drugs. The relationship between analgesia and the incidence of respiratory upset is discussed later. There was no marked difference between

TABLE III

Physical characteristics of patients, details of operations and average induction dose of methohexitone in the series under study.

Drug	Dose (mg)	No. of cases	Average age (yrs.)	Average weight (kg)	Average duration (min)		Av. induction dose of methohexitone (mg/kg)	Percentage incidence of dilatation of cervix
					Anaesthesia	Operation		
Chlorpromazine	20–50	19	34.53 ± 2.87	57.90 ± 3.97	10.3	8.1	1.60	63
Promazine	100	22	30.81 ± 1.58	58.86 ± 3.56	8.3	6.6	1.58 ± 0.05	64
Promazine	25	31	34.55 ± 1.75	59.39 ± 2.51	8.8	7.1	1.61 ± 0.05	45
Total Promazine	25–100	53	33.00 ± 1.24	59.15 ± 1.65	8.6	6.9	1.60 ± 0.03	53
Trimeprazine	25	10	31.8	60.6	7.1	5.6	1.57	50
Prochlorperazine	12.5	34	32.18 ± 0.86	57.64 ± 1.56	8.9	6.3	1.61 ± 0.04	82
Perphenazine	5	38	31.39 ± 1.35	60.10 ± 1.72	8.4	6.9	1.56 ± 0.3	71
Trifluperazine	1	11	31.2	54.3	7.2	6.0	1.61	64
Triflupromazine	20	34	29.9 ± 1.40	55.78 ± 1.33	8.4	6.6	1.58 ± 0.02	82
Promethazine	50	37	30.97 ± 1.36	56.35 ± 0.52	10.1	8.1	1.60 ± 0.02	73
Promethazine	10	36	35.78 ± 0.41	59.39 ± 0.67	8.2	6.8	1.55 ± 0.03	28
Total Promethazine	10–50	73	32.52 ± 1.13	57.36 ± 1.35	9.1	7.6	1.57 ± 0.01	51
Pecazine	50	24	30.63 ± 2.24	61.42 ± 4.10	9.2	7.9	1.58	63
Control data								
Atropine	0.6	100	34.59 ± 1.19	57.44 ± 1.18	10.4	8.5	1.60 ± 0.02	50
Pethidine	100	100	30.48 ± 0.09	55.57 ± 0.13	9.0	7.4	1.59 ± 0.003	50

TABLE IV

Percentage incidence of complications recorded during methohexitone anaesthesia with different premedicant drugs.

Pre-anaesthetic medication and dosage in mg	No. of pts.	Excitatory phenomena			Respiratory upset			Mar'd resp. depn.	Degree of hypotension (mm/hg)			Duration of hypotension (min)*			Grade of anaesthesia		
		Tremor	I.M.M.	Nil	C/H	L	Nil		−20	21—40	41+	−5	5—10	10+	1	2	3
Chlorpromazine 25–50	19	16	26	65	31	5	64	5	53	37	10	33	33	33	31	58	11
Promazine 100	22	14	23	73	32	0	68	0	77	18	5	60	40	0	41	54	5
Promazine 25	31	0	16	84	10	3	87	0	58	39	3	77	15	8	58	42	0
Trimeprazine 25	10	30	20	70	10	0	90	0	40	20	40	17	83	0	30	40	30
Prochlorperazine 12.5	34	9	35	59	21	0	79	0	73	12	15	56	33	11	50	44	6
Perphenazine 5	38	13	24	66	18	11	79	0	58	26	16	37	50	13	50	37	13
Trifluperazine 1	11	18	36	55	45	36	55	0	73	18	9	67	33	0	18	55	27
Triflupromazine 20	34	12	29	71	21	6	79	0	88	12	0	50	50	0	62	26	12
Promethazine 50	37	51	62	19	38	3	59	0	73	11	16	50	30	20	14	46	40
Promethazine 10	36	22	58	39	39	19	56	3	75	19	6	44	56	0	28	56	16
Pecazine 50	24	33	67	29	28	4	58	4	79	17	4	60	40	0	17	46	37
Control data																	
Atropine 0.6	100	16	14	73	27	3	72	2	87	8	5	54	46	0	57	37	6
Pethidine 100	100	1	6	93	13	3	84	8	89	10	1	55	36	9	72	27	1

*Calculated from number of patients having falls in systolic pressure in excess of 20 mm Hg.

I.M.M. = Involuntary muscle movements. C/H = Cough or hiccough. L = Laryngospasm.

the effects of the different doses of either promazine or promethazine.

Table IV shows that none of the phenothiazine derivatives had any appreciable effect on the respiratory depressant action of 1.6 mg/kg methohexitone.

In a recently published textbook, Foster (1959) claims that the use of promethazine prevents such disturbances as bucking, coughing and spasm during anaesthesia. Previous writers have noted that this drug makes laryngeal reflexes less active (Dinnick, 1954; Hopkin, Hunter and Jones, 1957); enables endotracheal tubes to be better tolerated (Harrison, 1955); and relieves bronchospasm (Loyn, 1956; Watkinson, 1960). Hunter (1958) has made similar claims for the action of pecazine. Although endotracheal intubation was not carried out in any of the patients in this study, there was no evidence of a depressant action of the phenothiazine derivatives on respiratory tract reflexes. In fact, the drug for which most claims have been made proved to be one of the least satisfactory as regards the incidence of coughing and hiccough. It must be remembered that these data were obtained using a barbiturate which is associated with a higher incidence of respiratory upset than thiopentone. A more likely explanation for the findings is the absence of pethidine or pethidine or similar drugs in the premedication. As with many other aspects of the actions of phenothiazine derivatives, beneficial effects have been ascribed to them which may, in fact, be due to the large doses of analgesics with which they are frequently combined.

Hypotension.

Too few patients were premedicated with trimeprazine and trifluperazine to enable conclusions to be drawn from the data. These are excluded from the discussion. The data in table IV are

TABLE V

Further analysis of the hypotensive action of a standard dose (1.67 mg/kg) of methohexitone with various forms of premedication.

Pre-anaesthetic medication	Dose (mg)	Mean fall in systolic blood pressure (mm Hg)	Patients with significant degree of hypotension				
			Percentage incidence	Comparison with incidence following atropine alone		Average degree of fall (mm Hg)	Average duration of fall (min)
				χ^2	P		
Atropine	0.6	13.4±0.9	13			35.3	4.8
Chlorpromazine	25–50	21.1±2.9	47	12.13	<0.001	33.3	7.7
Promazine	100	15.2±2.2	23	16.21	<0.001	33.0	4.6
Promazine	25	18.9±1.9	42	13.19	<0.001	31.1	4.4
Prochlorperazine	12.5	17.5±2.2	27	3.55	<0.10	38.3	5.4
Perphenazine	5	20.8±2.2	42	13.99	<0.001	35.6	7.6
Triflupromazine	20	11.7±1.3	12	0.37	<0.70	30.0	4.8
Promethazine	50	17.8±2.2	27	4.32	<0.05	39.0	6.2
Promethazine	10	15.8±1.8	25	2.47	<0.20	33.3	5.2
Pecazine	50	14.8±2.0	21	0.52	<0.50	33.0	5.8

TABLE VI

Subdivision of phenothiazine derivatives into chemical groups and comparison of the frequency and degree of hypotension following the injection of methohexitone (1.67 mg/kg) in patients premedicated with the members of these groups.

	Comparison of different side chains		Comparison of chlorinated and non-chlorinated	
	Dimethyl amino propyl	Piperazine	Chlorinated	Non-chlorinated
% Frequency of marked hypotension	27.9	29.9	37.3	24.0
Difference	$\chi^2 = 0.83$ P < 0.50		$\chi^2 = 16.312$ P < 0.001	
Mean fall in systolic pressure (mm Hg)	16.6±0.84	19.2±1.59	19.6±0.8	15.7±1.4
Difference	t = 1.44 0.20 > P > 0.10		t = 2.31 P < 0.05	

further analyzed in table VI. With the exception of trifluprομazine and pecazine, premedication with any of the phenothiazine derivatives increased the extent to which the systolic blood pressure fell after injection of the standard induction dose of methohexitone, compared with the changes observed in patients who received atropine alone. The incidence of patients in whom the fall in pressure did not exceed 20 mm Hg was not significantly increased by premedication with prochlorperazine 12.5 mg, trifluprομazine 20 mg, promethazine 10 mg or pecazine 50 mg, but was increased with the other drugs. The figures for average degree of hypotension and the duration of blood pressure fall are based on too few observations to permit statistical evaluation.

Reduction of the dose of promethazine from 50 to 10 mg decreased the frequency and severity of hypotension during the course of the subsequent anaesthesia. This did not apply with the lower (25-mg) dose of promazine, which produced a slightly greater degree of hypotension than the 100-mg dose. The difference between the effects of the two doses of either drug did not reach the accepted levels of significance.

The data were further analyzed to find if any one particular group of phenothiazine derivatives was more prone to cause hypotension than the others. No relationship could be demonstrated between analgesic action and effect on methohexitone-induced blood pressure falls. This also applied when the compounds with dimethylaminopropyl side chains were grouped together and the effects compared with those of the piperazine side chain drugs (table VI).

It will be recalled that severe degrees of hypotension were frequently encountered before and after operation in patients who received chlorpromazine 50 mg or prochlorperazine 25 mg. This led to a comparison of the degree and frequency of hypotension in patients premedicated with chlorinated and non-chlorinated phenothiazine derivatives. It was not surprising to find a significant difference between these groups (table VI). Too much importance must not be attached to this finding since this is not a comparison between otherwise identical chlorinated and non-chlorinated phenothiazine derivatives. Furthermore, the nonchlorinated group includes trifluprομazine, and since fluorine reduces the toxicity of other compounds, this may have unduly biased the results.

Despite the paucity of observations with chlorpromazine, it was considered worth while to compare the degree and severity of hypotension which followed in patients premedicated with promazine (pooled data for 100-mg and 25-mg doses) and its chlorinated and trifluorinated analogues. The findings, which are set out in table VII show that premedication with trifluprομazine is associated with less hypotension during anaesthesia than is premedication with either of the other two compounds. With the small amount of data available, it was not possible to demonstrate any significant difference between the effects of chlorpromazine and promazine.

It would be quite impracticable to discuss all the published work on the hypotensive action of phenothiazine derivatives, even in relation to barbiturate anaesthesia only. Some relevant publications will be briefly reviewed. There seems to be unanimity of opinion as regards the hypotensive action of chlorpromazine (Russell, 1956; Kvisselgaard, 1958) which is present even with small doses (Dripps et al., 1955; Etsten and Li, 1957). When used in premedication it increases blood pressure falls during thiopentone anaesthesia (Dripps et al., 1955; Dundee, 1958). The work of Eckenhoff, Helrich and Rolph (1957), Millar (1957) and Bergner and Ma (1960) also showed that promethazine has less hypotensive action than chlorpromazine. Eggers, Corssen and

TABLE VII

The results of statistical comparison of the extent of hypotension which was observed in patients premedicated with promazine, chlorpromazine and trifluprομazine.

Drugs compared	Frequency of hypotension	Mean fall in systolic B.P.
Promazine and chlorpromazine	$\chi^2 = 1.345$; $0.30 > P > 0.20$	$t = 1.16$: df = 70 : $0.30 > P > 0.20$
Promazine and trifluprομazine	$\chi^2 = 5.189$; $P < 0.05$	$t = 5.40$: df = 53 : $P < 0.001$
Chlorpromazine and trifluprομazine	$\chi^2 = 6.957$; $P < 0.01$	$t = 2.99$: df = 51 : $P < 0.01$

Allen (1959) attribute this difference to a weaker adrenolytic action. They also found that the adrenolytic action of pecazine is intermediate between that of chlorpromazine and that of promethazine. Several reports suggest that clinical doses of pecazine do not frequently produce hypotension (Mignault, 1957; Williams, 1957; Hooper, 1958), even when given intravenously during anaesthesia (Kavan et al., 1959).

In a comparative study of various phenothiazine premedicants prior to thiopentone anaesthesia, Dobkin and Purkin (1960) noted too high an incidence of postinduction hypotension following the use of promazine 25 mg and prochlorperazine 5 mg but negligible effects following promethazine 25 mg. However, Lamphier (1959) observed no cardiovascular upset following the intramuscular injection of prochlorperazine 10 mg. Dobkin (1959) found that perphenazine 5 mg had no effect on blood pressure or pulse rate. This is supported by Phillips et al. (1958), who found that premedication with perphenazine 5 mg resulted in less hypotension during thiopentone, nitrous oxide and oxygen anaesthesia than did morphine 10 mg. Lear et al. (1959) noted a 14.5 per cent incidence of hypotension following intramuscular injection of 10 to 40-mg doses of trifluprazine and the frequency increased with age and with the addition of pethidine. This was contrary to the experience of Zeedick (1960), who observed no hypotension following the use of 20-mg doses.

Most of these findings parallel the authors' experiences as reported here. Considering both the duration and severity of hypotension, it was found that premedication with trifluprazine 20 mg or pecazine 50 mg was more satisfactory than with any of the other phenothiazine derivatives. It must not be forgotten, however, that all the seven remaining drugs significantly increased the hypotensive action of methohexitone.

Grades of anaesthesia.

The classification of grades employed in this study, was described originally by Dundee and Riding (1960), solely for application to the induction of anaesthesia. In this and similar studies in which the operations have been of a standard type and of short duration, it embraces the whole course of anaesthesia. By virtue of the criteria adopted (q.v.), it reflects on all the complications of the administration and is the final standard by which to judge the overall effect of the premedication.

Figure 3 shows that only two of the drugs produced as good or safe operating conditions as atropine alone (namely promazine 25 mg and trifluprazine 20 mg). With these two drugs neither the incidence of excitatory phenomena nor the severity or duration of hypotension was markedly increased. Prochlorperazine 12.5 mg and perphenazine 5 mg were almost as good but with both of these the average duration of hypotension was slightly greater than after atropine.

A useful method for expressing the significance of the frequency of grades of anaesthesia as a single figure, which reflects on the relative merits of the various phenothiazine derivatives as premedication agents is to subtract the percentage incidence of grade 3 anaesthesia from that of grade 1. The results of this calculation are set out below and the drugs are listed in order of merit.

Atropine alone	+51
Atropine + promazine 25 mg	+50
Atropine + trifluprazine 20 mg	+50
Atropine + prochlorperazine 12.5 mg	+46
Atropine + perphenazine 5 mg	+37
Atropine + promazine 100 mg	+36
Atropine + trimeprazine 25 mg	0
Atropine + trifluperazine 1 mg	− 9
Atropine + pecazine 50 mg	−11
Atropine + promethazine 10 mg	−12
Atropine + chlorpromazine 25–50 mg	−20
Atropine + promethazine 50 mg	−26

The ideal premedication given before the ideal intravenous anaesthetic would give a figure of +100. A combination which gives a negative figure is, by virtue of its method of calculation, unsuitable for routine clinical use. Since the value for pethidine premedication is +71, it would appear that it is to be preferred to any of the phenothiazine derivatives when methohexitone is to be used. When promethazine 50 mg and pethidine 100 mg were combined, Moore and Dundee (1961a) found a distribution of grades of anaesthesia which would give a value of +32. The present findings suggest that either promazine 25 mg or trifluprazine 20 mg should give better results when combined with pethidine 100 mg. Such a combination might have the benefits of the anti-emetic action of the phenothiazine derivatives and the analgesic properties of pethidine.

Dosage.

There have been many claims that the phenothiazine drugs potentiate the action of the barbiturates. The average total requirements of methohexitone have therefore been analyzed for each form of premedication with which there were sufficient cases to justify a comparison with the atropine and pethidine data. Table VIII shows that, with the exception of promethazine 50 mg and pecazine 50 mg, all the phenothiazine derivatives used in the study reduced the total dosage of methohexitone to a significant degree. Their effect on the frequency of supplementary doses of barbiturate was less marked and this was lowered to a significant degree only by chlorpromazine and promazine 25 mg. Premedication with promethazine 50 mg markedly increased the need for supplementary doses.

TABLE VIII

Data on total doses of methohexitone, with various premedicants.

Premedication	Percentage use of supplementary doses	cf Atropine		Average total dose	cf Atropine		cf Pethidine
		χ^2	P	mg/kg	t	P	P
Atropine 0.6 mg	84	—	—	2.68 ± 0.024	—	—	0.001
Pethidine 100 mg	66	37.84	0.001	2.06 ± 0.006	9.39	0.001	—
Chlorpromazine 25–50 mg	42	18.28	0.001	2.21 ± 0.172	2.24	0.02	0.50
Promazine 100 mg	77	0.43	0.70	2.07 ± 0.087	6.48	0.001	—
Promazine 25 mg	64	9.52	0.01	2.01 ± 0.005	4.14	0.01	0.70
Prochlorperazine 12.5 mg	71	3.11	0.10	2.17 ± 0.097	5.00	0.001	0.40
Perphenazine 5 mg	72	2.80	0.10	2.15 ± 0.081	2.03	0.05	0.40
Triflupromazine 20 mg	79	0.45	0.50	2.06 ± 0.073	4.89	0.001	—
Promethazine 50 mg	97	3.69	0.05	2.79 ± 0.089	1.16	0.30	0.001
Promethazine 10 mg	86	—	—	2.39 ± 0.085	2.18	0.05	0.01
Pecazine 50 mg	95	1.92	0.20	2.86 ± 0.125	0.54	0.60	0.001

As found previously, premedication with pethidine reduced the total requirements of methohexitone to a striking degree. None of the phenothiazine derivatives caused a significantly greater average reduction in dosage than pethidine and, as expected, the promethazine and pecazine patients required significantly more barbiturate than those who received analgesic.

In a study of the effect of hyoscine on methohexitone anaesthesia, Dundee and Moore (1961b) noted that, although this premedicant did not result in an overall reduction in total barbiturate dosage as compared with atropine, there was a significant difference in the requirements between the patients who did and did not exhibit excitatory phenomena. In the uncomplicated administrations, hyoscine significantly reduced total methohexital requirements but the opposite effect was noted in patients in whom muscle movements occurred. The authors concluded that any potentiating effect hyoscine might have was more than counterbalanced by the frequent necessity for large doses in attempts to control abnormal muscle movements.

It was therefore considered necessary to subdivide the phenothiazine data as described above (table IX). There was no detectable difference in the average total dosage of methohexitone, after atropine premedication, between patients in whom excitatory phenomena did and did not occur. However, such a difference occurred with most of the phenothiazine derivatives with which there were sufficient cases to make the comparison. With those drugs in which an overall reduction in dosage has already been demonstrated this did not occur in patients who exhibited excitatory phenomena. In the absence of excitatory phenomena, this reduction in dosage was very marked except after the use of promethazine and pecazine. With these drugs there was no significant difference from the control, irrespective of the occurrence of excitatory phenomena. Thus, while it is possible to attribute part of the failure to demonstrate an overall reduction in methohexitone requirements after promethazine and pecazine premedication to the very frequent need for high doses to control abnormal muscle movements, this is not the complete explanation.

TABLE IX

Further analysis of total methohexitone requirements, subdividing patients into those with and without excitatory phenomena. It was necessary to pool total promethazine cases to obtain sufficient numbers for a reliable statistical evaluation of the findings.

	Patients with excitatory phenomena			Patients with no excitatory phenomena		
	Percentage incidence	Average dose (mg/kg)	cf Atropine	Average dose (mg/kg)	cf Atropine	Difference between groups of patients
Atropine 0.6 mg	27	2.73 ± 0.223		2.29 ± 0.074		t = 1.88 : P < 0.10
Promazine 100 mg	27	2.24		1.99 ± 0.072	t = 2.57 : P < 0.02	
Promazine 25 mg	16	2.42		1.89 ± 0.070	t = 3.65 : P < 0.001	
Total Promazine	21	2.32 ± 0.108	t = 1.60 : P < 0.20	1.90 ± 0.073	t = 3.25 : P < 0.001	t = 3.31 : P < 0.01
Prochlorperazine 12.5 mg	41	2.37 ± 0.121	t = 0.61 : P < 0.60	2.03 ± 0.139	t = 2.22 : P < 0.05	t = 1.90 : P < 0.10
Triflupromazine 20 mg	29	2.20		1.96 ± 0.050	t = 3.00 : P < 0.01	
Perphenazine 5 mg	34	2.43 ± 0.149	t = 1.15 : P < 0.30	2.00 ± 0.071	t = 2.83 : P < 0.01	t = 2.69 : P < 0.01
Promethazine 50 mg	81	2.90 ± 0.100	t = 0.44 : P < 0.50	2.40 ± 0.160	t = 1.69 : P < 0.10	t = 2.32 : P < 0.05
Promethazine 10 mg	61	2.49 ± 0.111	t = 0.95 : P < 0.40	2.09 ± 0.140	t = 0.33 : P < 0.80	t = 1.89 : P < 0.10
Total Promethazine	71	2.73 ± 0.102		2.25 ± 0.115		t = 2.89 : P < 0.01
Pecazine 50 mg	71	3.02 ± 0.134	t = 1.58 : P < 0.20	2.46 ± 0.090	t = 1.03 : P < 0.40	t = 3.17 : P < 0.01

Table X lists the frequency of awake, safe and unsafe patients 2 minutes after the end of anaesthesia. Omitting those series in which the overall requirements of methohexitone were not lower than for atropine (promethazine 50 mg and mepazine 50 mg), this table suggests that the remaining drugs, except perphenazine and trifluprazine prolong barbiturate narcosis.

None of these observations, with the exception of those relating to promethazine and pecazine, are contrary to accepted views. Animal experiments by Courvoisier et al. (1953), Burn (1954) and Dundee and Scott (1958) demonstrated that chlorpromazine prolonged barbiturate narcosis.

TABLE X

Condition of patients at end of methohexitone anaesthesia with forms of premedication.

Premedication (mg)	Percentage incidence of condition of patients 2 minutes after the end of anaesthesia		
	Awake	Safe	Unsafe
Atropine 0.6	72	27	1
Pethidine 100	68	25	7
Chlorpromazine 25—30	42	47	11
Promazine 100	41	54	5
Promazine 25	58	42	0
Prochlorperazine 12.5	52	48	0
Perphenazine 5	65	32	3
Trifluprazine 20	74	26	0
Promethazine 50	46	54	0
Promethazine 10	44	56	0
Pecazine 50	50	50	0

Sadove, Balagot and Reyes (1956) found that it "deepened" the state of anaesthesia as judged by the electroencephalogram. However, none of these workers were able to demonstrate as marked an action with promethazine. More recently, Dobkin (1960) demonstrated a prolongation of thiopentone narcosis by promazine in the dog but he was unable to detect any such effect after prochlorperazine, trifluperazine or pecazine. Although his studies did not include chlorpromazine, he stated in a previous paper that promazine was about half as effective as chlorpromazine in potentiating anaesthetics (Dobkin, 1958).

Clinical observations by Dripps et al. (1955) detected a reduction in thiopentone dosage in patients premedicated with chlorpromazine but they considered this to be an additive effect rather than a true potentiation. Dryberg and Johannsen (1958) found no difference between thiopentone requirements after chlorpromazine 50 mg or morphine 10 mg but they did not compare their data with atropine controls. Contrary to our findings are those of Blundell et al. (1959) and Haselhuhn and Brunson (1959), who stated that a 20 to 50 per cent reduction in thiopentone requirements occurred after promethazine premedication. The present authors are unable to offer any explanation for the difference in their own results. It cannot be attributed to the use of a different barbiturate, for in an earlier study carried out on identical lines, Moore and Dundee

(1961a) could not demonstrate any reduction in thiopentone dosage after promethazine.

Sequelae.

It is not the purpose of this study to investigate the relative anti-emetic properties of the phenothiazine derivatives but the available data will be discussed briefly. Riding (1960) found that dilatation of the cervix increased the incidence of postoperative vomiting and/or nausea as compared with patients who only had a curettage. He considers that the difference in his results is probably accounted for by the longer time required for the operation of dilatation and curettage (personal communication). The numbers of cases premedicated with each individual phenothiazine derivative are too small to justify subdivision into the above groups, so the control data have been examined (atropine and pethidine figures; table XI). It was found that they did not agree with Riding's finding, presumably because there was a similar duration of anaesthesia for both operations. The authors felt justified, therefore, in pooling the data from both operations in the phenothiazine series. Table XI demonstrates the very low incidence of nausea or vomiting with each of the drugs studied. When these were pooled together, there was no difference between the incidence with the two types of operation but there was a significant increase in the number of patients who had no emetic sequelae, as compared with atropine ($P<0.02$) or pethidine ($P<0.001$).

TABLE XI

Incidence of nausea and vomiting during first 6 hours after anaesthesia.

Pre-anaesthetic medication	Nausea and vomiting	Nausea only	Nil
Atropine 0.6 mg (D & C)	18	8	74
Atropine 0.6 mg (C)	20	14	66
Atropine 0.6 mg (Total)	19	11	70
Pethidine 100 mg (D & C)	16	26	58
Pethidine 100 mg (C)	38	10	52
Pethidine 100 mg (Total)	27	18	55
Chlorpromazine 25—30 mg	11	0	89
Promazine 100 mg	9	9	82
Promazine 25 mg	15	6	79
Prochlorperazine 12.5 mg	9	3	88
Perphenazine 5 mg	7	0	93
Triflupromazine 20 mg	11	3	86
Promethazine 50 mg	24	8	68
Promethazine 10 mg	6	6	82
Total Phenothiazines (D & C)	13	5	82
Total Phenothiazines (C)	8	6	86
Total Phenothiazines (Total)	11	6	83

D & C = Dilatation and curettage.
C = Curettage alone.

Although restlessness occurred before the induction of anaesthesia with all drugs, this was not observed after operation. One patient, premedicated with perphenazine 5 mg developed pseudo-Parkinsonism after operation. Athetoid movements of the hands were noted before anaesthesia, which became worse in the postoperative period. Soluble phenobarbitone 200 mg was given 90 minutes after operation and produced a remission of symptoms. A similar incident has been reported by Robbie (1959) but the authors have not observed it with any other drug. Amnesia was not a feature of any of the administrations.

Hypotension with prochlorperazine, chlorpromazine and trimeprazine has already been referred to, and this necessitated a reduction of dosage with the former two drugs and abandonment of the study of the latter. With the reduced dosage it did not occur in the postoperative period.

DISCUSSION

It has been obvious throughout this investigation that some relationship exists between the analgesic action of the phenothiazine derivatives and their effect on the course of methohexitone anaesthesia. This applies particularly to the incidence of excitatory phenomena and to the total dosage of barbiturate required for the standard operation.

In figure 4 the incidence of excitatory phenomena has been plotted against the analgesic indices. Pethidine is included for comparison. This confirms that the more anti-analgesic drugs are associated with higher incidences of this complication. Grouping the compounds as discussed earlier the overall incidences of excitatory phenomena were found to be as follows:

Group 1: some analgesic action 25 per cent.
Group 2: mildly anti-analgesic 36 per cent.
Group 3: strongly anti-analgesic 69 per cent.

There is a highly significant difference between the incidence with each of the three groups. However, not even with group 1 is the frequency of this complication as low as after the use of pethidine ($P<0.001$).

It was not possible to demonstrate such a close

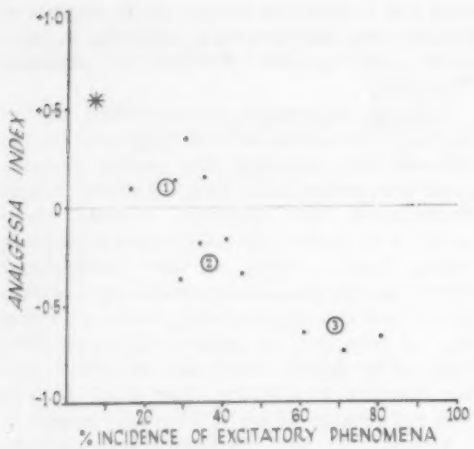


FIG. 4

Correlation between the analgesia index of the premedication and the incidence of excitatory phenomena associated with methohexitone anaesthesia. Dots refer to individual phenothiazine derivatives while circles refer to pooled data for groups as outlined in text.
* = Pethidine 100 mg.

correlation between the analgesic activity of the phenothiazine derivatives and the incidence of respiratory upset associated with their use in premedication. This complication occurred in 22 per cent of group 1 cases and in 24 per cent in group 2. Both these differed significantly ($P<0.01$) from the 42 per cent incidence in group 3.

As regards dosage, it was found that the markedly anti-analgesic phenothiazines (promethazine, pecazine) did not decrease the total requirements of methohexitone, compared with the atropine control series, whereas a significant reduction was found after the use of all the other drugs (table VIII). Even in patients who did not exhibit excitatory phenomena it was not possible to demonstrate a reduction in dosage (table IX) following these two phenothiazine derivatives. In addition they increased the frequency of need for supplementary doses of methohexitone. This suggests the possibility of some antagonism between the phenothiazine derivatives under consideration and the anaesthetic state.

Methohexitone is an ideal drug for studies of this nature, being unique among the intravenous barbiturates in current clinical use in regard to the degree to which the course of anaesthesia can be affected by premedication. Dundee and Moore (1961b) have found that another "anti-analgesic" pre-anaesthetic drug (hyoscine 0.4 mg) has an action qualitatively similar to that of promethazine and pecazine. In unpublished studies a similar effect has been detected after the use of cyclizine 50 mg (analgesia index −0.49).

It would be unjustifiable to assume that these findings apply to thiopentone, with which the incidence of complications is normally much lower than with methohexitone. However, Moore and Dundee (1961a) found that premedication with promethazine 50 mg adversely affected the course of thiopentone anaesthesia in a similar manner but to a lesser extent than methohexitone.

Probably the most important clinical application of the present findings is the demonstration of markedly varying effects following the use of different phenothiazine derivatives. These differences do not seem to be generally appreciated judging by the many reports of "phenothiazine premedication" which do not specify the use of a particular drug. It is well known that minor alterations in the barbiturate nucleus can have a profound effect on clinical action and this work shows that the same applies to the phenothiazine group. While the importance of various radicles attached to the barbiturate ring is fairly well known, this cannot be said for the group under study. Our results suggest that chlorination or fluorination may affect their hypotensive action, but no chemical explanation can be offered for their varying analgesic or anti-analgesic activity.

SUMMARY AND CONCLUSIONS

Previous experiences with methohexitone have shown that both the incidence and severity of side effects following injection are markedly affected by the pre-anaesthetic medication. Analgesic drugs were found to decrease the incidence of spontaneous movement, whereas compounds which increase sensitivity to pain had the opposite effect. However, these observations were made with compounds of widely dissimilar chemical structure and it was felt that a study using drugs with a common nucleus, but which differed in the structure of their side chains and in their

analgesic activity would be of value. The phenothiazines are such a group.

Using a standard anaesthetic technique for the operation of dilatation and curettage and determining the optimum number of cases by the method of sequential analysis, it was found that the markedly anti-analgesic phenothiazine derivatives significantly increase the frequency of excitatory phenomena during methohexitone anaesthesia. They have a less marked effect on the frequency of respiratory upset with the same drug.

All the phenothiazine derivatives studied with the exception of trifluprómazine and pecazine, increased the hypotensive effect of a standard induction dose of methohexitone. There is suggestive evidence that chlorination increases and fluorination decreases the hypotensive action of the phenothiazine derivatives.

A marked reduction in total dosage of methohexitone required for the standard operation was observed with all the phenothiazine derivatives, excepting those with a marked anti-analgesic action. Premedication with pethidine also significantly reduced total barbiturate requirements.

These findings stress the importance of analgesic premedication before the use of methohexitone and suggest that the phenothiazine derivatives are not the best drugs to use before this barbiturate is injected.

ACKNOWLEDGMENTS

We are grateful to Mr. I. H. McClure and the staff of the gynaecological department of Musgrave Park Hospital for their co-operation in this investigation. Thanks are also due to Mr. S. J. Kilpatrick for preparing the sequential plans and Mr. G. A. Smith for the illustrations. Generous supplies of drugs were provided as follows: methohexitone (Brietal) by Eli Lilly and Co.; promethazine (Phenergan), chlorpromazine (Largactil), trimeprazine (Vallergan) and prochlorperazine (Stemetil) by May and Baker Ltd.; trifluprómazine (Vespral) by E. R. Squibb; promazine (Sparine) by John Wyeth and Bro.; perphenazine (Fentazin) by Allen and Hanbury Ltd.; and trifluperazine (Stelazine) by Smith, Kline and French Laboratories.

REFERENCES

Adelman, M. H., Jacobson, E., Lief, P. A., and Miller, S. A. (1959). Promethazine hydrochloride in surgery and obstetrics. *J. Amer. med. Ass.*, **169**, 5.

Barron, D. W., and Dundee, J. W. (1961). The recently introduced rapidly-acting barbiturates: a review and clinical appraisal in relation to thiopentone. *Brit. J. Anaesth.*, **33**, 81.

Bergner, R. P., and Ma, D. (1960). The circulatory effects of promethazine during spinal anesthesia. *Curr. Res. Anesth.*, **39**, 46.

Blundell, A. E., Pillion, S. W., Bodell, B., and Ansbro, F. P. (1959). Promethazine—an adaptable adjunct in anesthesia. *Curr. Res. Anesth.*, **38**, 328.

Burn, J. H. (1954). The pharmacology of chlorpromazine and promethazine. *Proc. R. Soc. Med.*, **47**, 617.

Courvoisier, S., Fournel, J., Ducrot, R., Kolsky, M., and Koetschet, P. (1953). Propriétés pharmacodynamiques du chlorhydrate de chloro-3 (diméthylamino-3 propyl)-10 phenothiazine (4560 R.P.); étude expérimentale d'un nouveau corps utilisé dans l'anesthesie potentialisée et dans l'hibernation artificielle. *Arch. int. Pharmacodyn.*, **92**, 305.

Dinnick, O. P. (1954). Discussion on paper on antihistamines in anaesthesia. *Proc. R. Soc. Med.*, **47**, 415.

Dundee, J. W. (1958). Iatrogenic disease in anaesthesia. *Brit. med. J.*, **1**, 1433.

—— Moore, J. (1960). Alterations in response to somatic pain. I: The evaluation of a method of analgesimetry. *Brit. J. Anaesth.*, **32**, 396

—— —— (1961a). Thiopentone and methohexital; a comparison as main anaesthetic agents for a standard operation. *Anaesthesia*, **16**, 50.

—— —— (1961b). The effect of scopolamine on methohexital anaesthesia. *Anaesthesia*, **16** (in press).

—— Riding, J. E. (1960). A comparison of Inactin and thiopentone as intravenous anaesthetics. *Brit. J. Anaesth.*, **32**, 206.

—— Scott, W. E. B. (1958). The effect of phenothiazine derivatives in thiobarbiturate narcosis. *Curr. Res. Anesth.*, **37**, 13.

Dobkin, A. B. (1958). Efficacy of ataractic drugs in clinical anaesthesia. *Canad. Anaesth. Soc. J.*, **5**, 176.

—— (1959). Perphenazine in clinical anaesthesia. *Canad. Anaesth. Soc. J.*, **6**, 341.

—— (1960). Potentiation of thiopentone anesthesia by derivatives and analogues of phenothiazine. *Anesthesiology*, **21**, 292.

—— Purkin (1960). Double blind study of phenothiazines used in pre-anaesthetic medication: a clinical evaluation of promethazine, promazine, prochlorperazine and levomepromazine. *Canad. Anaesth. Soc. J.*, **7**, 158.

Dripps, R. D., Vandam, L. D., Pierce, E. C., Oech, S. R., and Lurie, A. A. (1955). The use of chlorpromazine in anesthesia and surgery. *Ann. Surg.*, **142**, 774.

Dryberg, V., and Johannsen, S. H. (1958). Pre-anaesthetic medication with chlorpromazine (a comparison with morphine). *Acta Anaesth. scand.*, **2**, 133.

Eckenhoff, J. E., Helrich, M., and Rolph, W. D. (1957). The effects of promethazine upon respiration and circulation in man. *Anesthesiology*, **18**, 703.

Eggers, G. W. M., Corssen, G., and Allen, C. R. (1959). Comparison of vasopressor responses in the presence of phenothiazine derivatives. *Anesthesiology*, **20**, 261.

Etsten, B., and Li, T. H. (1957). Circulatory effects of chlorpromazine before and during cyclopropane anesthesia in man. *Anesthesiology*, **18**, 203.

Foster, C. A. (1959). The antihistamine and tranquilliser or ataractic drugs. *A Practice of Anaesthesia*, Ch. XXV, p. 707. W. D. Wylie and H. C. Churchill-Davidson. London: Lloyd-Luke.

Harrison, G. (1955). Phenothiazine derivatives in anaesthesia. *Brit. J. Anaesth.*, **27**, 131.

Haselhuhn, D. H., and Brunson, E. G. (1959). Promethazine hydrochloride as a supplement to anesthesia. *Curr. Res. Anesth.*, **38**, 429.

Hopkin, D. A. B., Hunter, D., and Jones, C. M. (1957). Promethazine and pethidine in anaesthesia. *Anaesthesia*, **12**, 276.

Hooper, E. R. S. (1958). Pecazine in abdominal surgery. *Brit. J. Anaesth.*, **30**, 528.

Hunter, A. R. (1958). Pacatal in neurosurgical anaesthesia. *Anaesthesia*, **13**, 379.

Jolly, C. (1960). Recovery time from methohexital anaesthesia. *Brit. J. Anaesth.*, **32**, 576.

Kavan, E. M., Brechner, V. L., Dillon, J. B., and Parker, L. A. (1959). Supplementation of nitrous oxygen—thiobarbiturate anesthesia with Pacatal. *Curr. Res. Anesth.*, **38**, 75.

Kvisselgaard, N. (1958). Chlorpromazine and chlorcyclizine in the prevention of post-operative nausea and vomiting. *Acta Anaesth. scand.*, **2**, 153.

Lamphier, T. A. (1959). The use of prochlorperazine in surgery. *J. Maine med. Ass.*, **50**, 8.

Lear, E., Suntay, R., Chiron, A. E., Pallin, I. M., Fisch, H., and Abrams, C. (1959). Tranquillisers in anesthesia: double blind studies. I: Trifluopromazine. *N.Y. St. J. Med.*, **59**, 3220.

Loyn, W. G. G. (1956). Promethazine in general anaesthesia. *Brit. J. Anaesth.*, **28**, 126.

Mignault (1957). Two years experience using the phenothiazine amine derivatives in anaesthesia and artificial hibernation with special mention of the new derivative Pacatal. *Canad. Anaesth. Soc. J.*, **4**, 37.

Millar, R. A. (1957). Promethazine and the circulatory response to tilting. *Canad. Anaesth. Soc. J.*, **4**, 364.

Moore, J., and Dundee, J. W. (1961a). Promethazine: its influence on the course of thiopentone and methohexital anaesthesia. *Anaesthesia*, **16**, 50.

—— —— (1961b). Alterations in response to somatic pain associated with anaesthesia. V: The effect of promethazine. *Brit. J. Anaesth.*, **33**, 3.

—— —— (1961c). Alterations in response to somatic pain associated with anaesthesia. VII: The effect of nine phenothiazine derivatives. *Brit. J. Anaesth.*, **33** (in press).

Phillips, O. C., Nelson, A. T., Lyons, W. B., Graff, T. D., and Frazier, T. M. (1958). The effect of Trilafon in post-anesthetic nausea, retching and vomiting. *Curr. Res. Anesth.*, **37**, 341.

Riding, J. E. (1960). Post-operative vomiting. *Proc. R. Soc. Med.*, **53**, 671.

Robbie, D. S. (1959). Post-anaesthetic vomiting and anti-emetic drugs. *Anaesthesia*, **14**, 349.

Russell, J. T. (1956). Chlorpromazine hydrochloride in anaesthesia. *S. Afr. med. J.*, **30**, 529.

Sadove, M. S., Balagot, R. C., and Reyes, R. M. (1956). The potentiating effect of chlorpromazine. *Curr. Res. Anesth.*, **35**, 165.

Stoelting, V. K. (1957). The use of a newer intravenous oxygen barbiturate 25398 for intravenous anesthesia. *Curr. Res. Anesth.*, **36**, 49.

Watkinson, M. S. (1960). Bronchospasm. (Correspondence.) *Anaesthesia*, **15**, 90.

Williams, H. (1957). Pacatal in anaesthesia. *N.Z. med. J.*, **56**, 41.

Wyant, G. M., and Chang, C. A. (1959). Sodium methohexital: a clinical study. *Canad. Anaesth. Soc. J.*, **6**, 40.

—— Barr, J. S. (1960). Further comparative studies of sodium methohexital. *Canad. Anaesth. Soc. J.*, **7**, 127.

Zeedick, J. F. (1960). Clinical investigation of trifluopromazine, hydrochloride (Vesprin) as pre-anesthetic medication. *Curr. Res. Anesth.*, **39**, 283.

Brit. J. Anaesth. (1961), **33**, 397

POSTOPERATIVE AMNESIA

BY

W. LAMBRECHTS* AND J. PARKHOUSE
Nuffield Department of Anaesthetics, University of Oxford, England

The modern anaesthetist tends to pride himself on having his patients awake before they leave the operating theatre. In many cases, however, this wakefulness means little more than an ability to respond to painful stimuli or shouted commands; it is often followed by a relapse into drowsiness, with amnesia of variable duration. Such amnesia is of no great consequence as long as the patient retains his protective reflexes but it is nevertheless of considerable interest. Patients may hold rational conversations with their relatives or may complain vociferously about pain or other discomforts and yet they may subsequently have no recollection of any of these things. This serves as a salutary reminder of the fact that the effects of our anaesthetic drugs by no means cease with the termination of surgery.

In one sense, Artusio's (1955) work with ether is no more than an advancement of the postoperative period to cover part of the operation itself. Indeed, it has been suggested to the authors (Watson, personal communication) that the logical conclusion of Artusio's work would be to give the patient his anaesthetic in the anaesthetic room and then perform the operation during the subsequent period of amnesia!

Records have been kept in order to obtain some information about postoperative amnesia and from these records it is possible to draw certain conclusions which may be of sufficient interest to warrant a brief communication.

METHOD

Patients were interviewed on the day following surgery, or later if necessary, and asked simply at what time they awoke from their anaesthetic. This often provided a fairly definite answer, since many patients ask the time, or look at a clock when they wake up. Thus, many patients were able to give a definite "endpoint" to their postoperative haziness or amnesia. In other cases, an approximate time could be fixed circumstantially, as, for example, teatime, or visiting time. There remained some patients who had no clear idea of their time of awakening and these patients have been listed separately.

It sometimes happens that a patient has an "island" of memory, or some vague recollection of an incident which may have been in real life or may have been a dream: in the analyses presented below such incidents have been included in the amnesic period, the waking time being considered to begin only from the recommencement of consequential recollections.

In addition to questioning of the patient, notes were kept of the premedication, anaesthetic agents, postoperative drugs, the time at which the patient arrived back in the ward and whether or not he was said by the anaesthetist to be awake on leaving the theatre.

RESULTS

Generally speaking, the extent of postoperative amnesia was found to vary tremendously from one patient to another. The factors which were thought to have a possible influence on the duration of amnesia will be discussed separately.

Age and premedication.

The patients in this series were premedicated in three ways: (1) with papaveretum and hyoscine; (2) with atropine and morphine, pethidine or promethazine; (3) with atropine alone. Patients premedicated with atropine alone were too few in number for worthwhile analysis.

A noticeable age difference was observable in the choice of premedication. Table I shows the numbers of patients in each decade who received premedication with papaveretum and hyoscine, and with atropine and an opiate or other sedative.

*Now at Groote Schuur Hospital, Cape Town, South Africa. Formerly Nuffield Dominion Clinical Assistant, Oxford.

TABLE I

Choice of premedication in relation to age of patient.

Age (years)	Hyoscine and papaveretum	Atropine and sedative	Total	Percentage atropine
Under 20	18	27	45	
20–	28	11	39	
30–	31	11	42	39.0
40–	31	17	48	
50–	26	20	46	
60–	4	23	27	
70–	0	19	19	92.0
80 and over	0	3	3	
Total	138	131	269	

Of 220 patients below the age of 60, 134 (61 per cent) received hyoscine and 86 (39 per cent) received atropine: of the patients over 60 years of age, 45 out of 49 (92 per cent) received atropine and no patient over 70 was premedicated with hyoscine.

In view of the well-known effect of hyoscine in producing amnesia, particularly for recent events, the influence of this drug, when used as a premedicant, was first of all investigated. Table II and figure 1 show the results of comparing atropine and hyoscine premedication in patients below the age of 60 who received no anaesthetic agents other than thiopentone and nitrous oxide: only patients stated by the anaesthetist to be awake on leaving the theatre, and only those who received no postoperative drug during the amnesic period were included. It may be seen that the preoperative use of hyoscine had a considerable influence on amnesia during the first few postoperative hours. Two hours after the end of operation, for example, 74 per cent of patients in the atropine group were "awake", compared with only 35 per cent in the hyoscine group. Statistically, these differences are highly significant.

The influence of age on postoperative amnesia was manifested through an increasing tendency to vagueness and inability to state a definite time of awakening, together with an increasing proportion of patients with long periods of amnesia (that is, in the "over 8 hours" group). This is well brought out by table III, which deals with patients filling the same criteria as those above, except that all ages were included and premedication in every case consisted of atropine and a sedative.

TABLE II

Influence of premedication on duration of amnesia.

All patients anaesthetized with thiopentone, nitrous oxide and oxygen. All stated to be awake on leaving the theatre. All below 60 years of age. No postoperative drugs given during amnesic period.

Premedication	Time of awaking						
	Less than 15 min	15 min –2 hr	2–5 hr	5–8 hr	Over 8 hr	No idea	Total
Atropine and sedative	28 (40.6%)	23 (33.3%)	12 (17.4%)	3 (4.4%)	1 (1.4%)	2 (2.9%)	69
Hyoscine and papaveretum	10 (10%)	25 (25%)	39 (39%)	19 (19%)	7 (7%)	0	100
Total	38	48	51	22	8	2	169

With 5–8 hour and over-8 hour groups added, and last column (patients with no idea of waking time) omitted, $\chi^2 = 39.9$; $n = 3$; $p < 0.01$.

TABLE III

Influence of age on duration of amnesia.

All patients anaesthetized with thiopentone, nitrous oxide and oxygen. All stated to be awake on leaving the theatre. All premedicated with atropine and morphine, pethidine or promethazine. No postoperative drugs given during amnesic period.

Age (years)	Duration of amnesia		
	Less than 8 hr	Over 8 hr or unknown	% over 8 hr or unknown
Under 40	43	6	12.1
40–	31	6	16.2
60–	16	7	30.4
70–	10	9	47.3
80 and over	0	3	100.0

The percentage of patients with over 8 hours postoperative amnesia, and with no idea of their awaking time, rose steadily with age to reach 47 per cent in the small group of patients between 70 and 80. Of the 3 patients over 80, none was able to state a time of awakening. The relationship between premedication, age, and difficulty in recalling the time of awaking will be referred to again in connection with postoperative drugs.

Anaesthetic agents.

In order to study the effect of different anaesthetic agents on postoperative amnesia, a comparison was made between nitrous oxide and oxygen, ether-air and trichloroethylene-air. Nitrous oxide and oxygen mixtures were administered with a standard circle absorber; ether-air and trichloroethylene-air mixtures were administered quantitatively by means of E.M.O. inhalers and the Oxford Inflating Bellows. In all cases premedication consisted of atropine and a sedative and minimal concentrations of the agent were used, usually in conjunction with muscle relaxant drugs. Again, the only patients included in the comparison were those stated by the anaesthetist to be awake at the end of the operation.*

The results of this comparison are shown in table IV and figure 2. The relative lack of amnesia in the first few hours after nitrous oxide was noticeable: 29 per cent of 130 patients receiving this agent had well-ordered memories from the moment of returning to bed, compared with no patients following trichloroethylene-air anaesthesia and only 1 patient out of 27 who received ether-air. Over 90 per cent of patients were able to state a definite time of awakening after both nitrous oxide and ether, but the trichloroethylene-air results were strikingly different, 10 of the 32 cases (31 per cent) being unable to give a definite time. Indeed, inspection of figure 2 reveals that

*Because of the small numbers of cases, patients of all ages were included in this comparison. The ether group contained a higher proportion of patients over the age of 60 (55.6 per cent) than either the nitrous oxide group (34.3 per cent) or the trichloroethylene group (37.5 per cent).

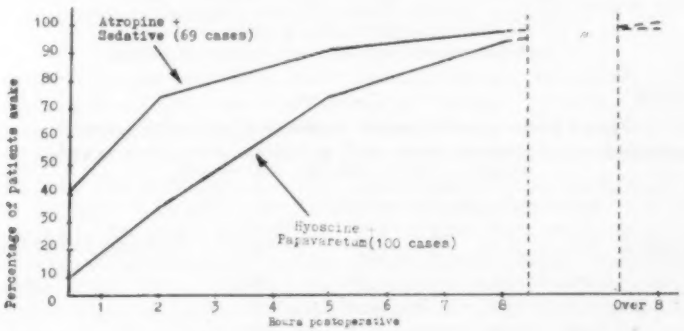


FIG. 1

Influence of premedication on duration of amnesia.
All patients anaesthetized with thiopentone, nitrous oxide and oxygen. All stated to be awake on leaving the theatre. All below 60 years of age. No postoperative drugs during amnesic period.

trichloroethylene was by far the most potent amnesia-producing agent of the three.

It should be made clear that the "over 8 hours" group extended indefinitely to include all patients who could state definitely when organized postoperative memory recommenced. After trichloroethylene-air anaesthesia, some of these times were remarkably long: for example, one young woman who received a trichloroethylene-air anaesthetic for a laparotomy had complete postoperative amnesia for 3 days, although she was awaking at the conclusion of surgery and appeared rational the following day. She was nevertheless able to give a perfectly clear endpoint to her period of amnesia and she was therefore included in the "over 8 hours" group.

Time of day.

The patients were placed in groups according to the time of their return from the operating theatre to the ward. It was felt that in this way it might be possible to relate the duration of postoperative amnesia to such factors as the patient's normal sleep rhythm and the general amount of activity and noise in the ward. Table V shows an analysis of 244 patients

TABLE IV

Influence of anaesthetic agent on duration of amnesia.

All patients premedicated with atropine and morphine, pethidine or promethazine. All stated to be awake on leaving operating theatre.

	Duration of amnesia											
Agent	Under 15 min	15 min–	1 hr–	2 hr–	3 hr–	4 hr–	5 hr–	6 hr–	7 hr–	8 hr+	No idea	Total
Nitrous oxide	38	15	19	8	7	8	4	1	0	12	18	130
Ether	1	1	4	3	3	2	0	2	2	9	0	27
Trichloroethylene	0	2	2	3	2	2	0	0	0	11	10	32
Total	39	18	25	14	12	12	4	3	2	32	28	189

	Hours of amnesia			
Agent	0–2	2–5	5+*	Total
Nitrous oxide	72	23	17	112
Trichloroethylene	4	7	11	22
Ether	6	8	13	27
Total	82	38	41	161

$\chi^2 = 30.1$; $n = 4$; $p < 0.01$.

* Excluding patients with unknown duration of amnesia.

TABLE V

Time of return to ward in relation to duration of postoperative amnesia.

All patients anaesthetized with thiopentone, nitrous oxide and oxygen. All stated to be awake on leaving operating theatre. M.N.—midnight; M.D.—midday.

	Hours of postoperative amnesia					
Time of return to ward	0–2	2–5	5–8	8+	Total no. patients	Percentage premedicated with atropine
M.N.–	6	7	7	0	20	50.0
6 A.M.–	9	10	8	6	33	45.4
M.D.–	48	26	11	9	94	42.6
6 P.M.–M.N.	52	28	11	6	97	49.0

With 5–8 hour group and over-8 hour group added together, $\chi^2 = 13.2$; $n = 6$; $0.05 > P > 0.02$.

With 5–8 hour group and over-8 hour group added together, and times of return divided into two 12-hour periods (M.N.–M.D. and M.D.–M.N.), $\chi^2 = 12.45$; $n = 2$; $p < 0.01$.

Premedication distribution: M.N.–M.D., 47.2 per cent atropine; M.D.–M.N., 45.9 per cent atropine.

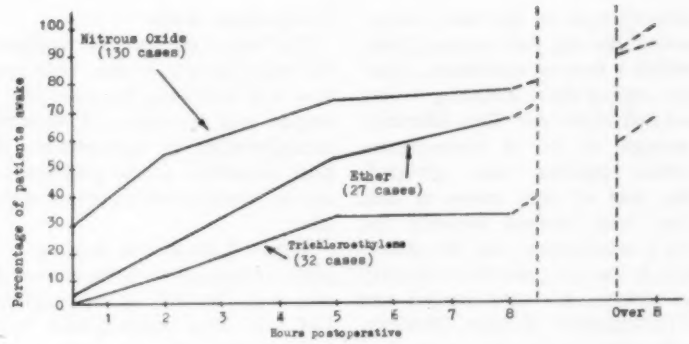


FIG. 2

Influence of anaesthetic agent on duration of amnesia.
All patients premedicated with atropine and morphine, pethidine or promethazine. All stated to be awake on leaving operating theatre.

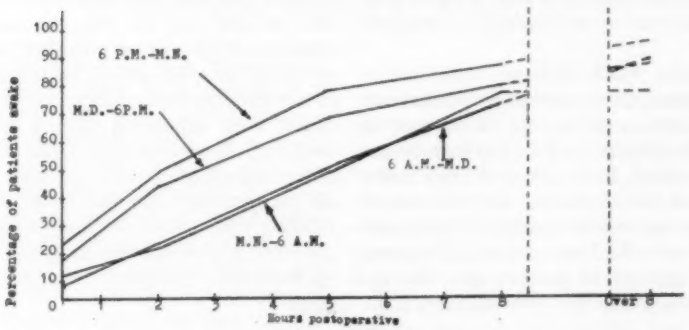


FIG. 3

Time of return to ward in relation to duration of postoperative amnesia.
All patients anaesthetized with thiopentone, nitrous oxide and oxygen. All stated to be awake on leaving operating theatre.

who were able to give a definite endpoint to their amnesia. Once again, only patients who received thiopentone, nitrous oxide and oxygen, and who were stated to be awake on leaving the operating theatre were included. The same data are presented graphically in figure 3, in which the time of the patient's return to the ward is divided into four periods of 6 hours. It can be seen that, other things being equal, there was a tendency for postoperative amnesia to be more prolonged during the first half of the day, and indeed if the first 12 hours of the day (from midnight to midday) are compared with the second 12 hours, a statistically significant difference is found to exist.

No entirely satisfactory explanation of this phenomenon can be offered, although there are several possible reasons. When patients are operated on late in the day it sometimes happens that premedication has been given well in advance; conversely, when patients are called for sooner than expected premedication is sometimes given only a little while before the induction of anaesthesia. It might well be supposed that if the premedication were given only a few minutes before anaesthesia a greater amount of postoperative "hangover" would result but it has not been possible to draw any conclusion about this from the present series. Of all patients anaesthetized with thiopentone and nitrous oxide and oxygen, and "awake" at the conclusion of surgery, 50 per

cent of those arriving back in the ward during the first 12 hours of the day had received their premedication within 1 hour of anaesthesia, compared with 39 per cent of those returning to bed during the second half of the day. This difference is not large enough to be of consequence. Furthermore, when patients were grouped, regardless of the time of their return to bed, according to the time interval between the administration of premedication and the induction of anaesthesia, it was not possible to establish any relationship between this time interval and the duration of postoperative amnesia. However, it may be that the present series is too small to permit of a sufficiently rigid control of the other variable factors. Reference to table V will show that the proportions of patients premedicated with papaveretum and hyoscine, and with atropine and a sedative did not vary greatly during the 24 hours of the day.

A further factor which must be considered is that many surgeons like to operate on old patients and poor-risk patients during the earlier part of the day and such patients are likely to have longer postoperative amnesia. In the group of cases under discussion, 12 of the 25 patients over the age of 60 were back in bed before midday (49 per cent) compared with only 22.3 per cent of all patients irrespective of age: of 10 patients over the age of 70, only 1 returned to bed after midday.

Postoperative drugs.

The longer the patient's postoperative amnesia, the more likely it is that some form of medication will intervene between the conclusion of surgery and the return of memory. Clearly, the administration of postoperative drugs may in itself contribute to the prolongation of amnesia, and an attempt was therefore made to study this effect.

Figure 4 shows the awaking times of patients who received nitrous oxide and oxygen anaesthesia, who were "awake" at the conclusion of surgery, and who were premedicated with papaveretum and hyoscine: these patients were placed in two groups according to whether or not they received a postoperative drug during their period of amnesia. Figure 5 shows a similar comparison in patients premedicated with atropine and a sedative. In each case the effect of intervening postoperative drugs was very marked but particularly so in the atropine group, in which 39 per cent of the patients who received postoperative medication were unable to state a definite time of awaking. As mentioned earlier, however, this group contained a relatively high proportion of old patients who often had no recollection of their awaking time: many of these patients received an intervening postoperative drug and their inclusion undoubtedly "weights" the lower curve of figure 5.

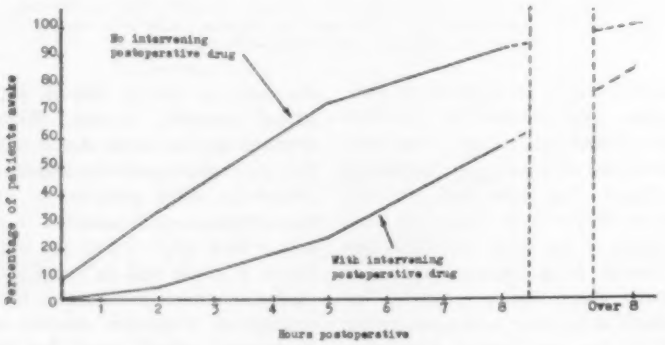


FIG. 4

Influence of postoperative drugs on duration of amnesia after hyoscine premedication.
All patients anaesthetized with thiopentone, nitrous oxide and oxygen. All stated to be awake on leaving operating theatre. All premedicated with papaveretum and hyoscine.

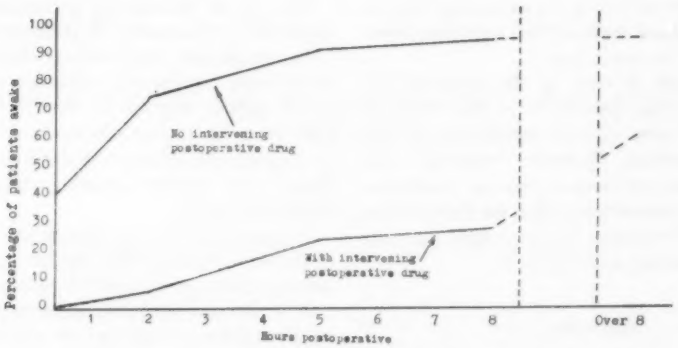


FIG. 5

Influence of postoperative drugs on duration of amnesia after atropine premedication.
All patients anaesthetized with thiopentone, nitrous oxide and oxygen.
All stated to be awake on leaving operating theatre. All premedicated with atropine and morphine, pethidine or promethazine.

In assessing the importance of a postoperative drug in prolonging amnesia, it is important to know the interval of time which elapses between administration of the drug and return of memory. If this interval is less than half an hour, for example, it may safely be concluded that the postoperative drug had no influence on the duration of amnesia. In the present series, of a total of 55 patients who received postoperative drugs and who were still able to state a definite time of awaking, the intervening period was less than 30 minutes in only 10 (18.1 per cent). In some patients more than one postoperative injection was given during the amnesic period, and in these the return of memory was often delayed for many hours.

Sex and duration of operation.

There was no evidence in the present series that the sex of the patient made any difference to the extent of postoperative amnesia.

The operations were classified according to their duration and severity but, again, there was no evidence that either of these factors was of significance. However, in the present series only 8 operations lasted for more than 2 hours and only 2 for more than 3 hours; it is quite possible that in a large series of very long operations the duration of anaesthesia might be found to have a significant influence on the duration of postoperative amnesia.

DISCUSSION

Scientific accuracy can never be expected from a study of this kind since the data are largely derived from the patient's own impressions. Innumerable factors are involved in the production of postoperative amnesia, and in the present paper an attempt has been made only to evaluate some of the more obvious ones which relate to premedication, anaesthetic agents and postoperative drugs.

It is quite evident from this small series of cases that the patient's impression of how soon he wakes up after an anaesthetic is likely to be very different from the anaesthetist's. Although many patients may be roused sufficiently to obey commands and to appear quite wakeful during the application of dressings at the conclusion of surgery, these patients sometimes fall asleep again on return to the ward. In the case of old, debilitated patients this recurrence of drowsiness may progress to the stage of a dangerous loss of protective reflexes. Patients who remain awake and who appear rational in their behaviour may have no subsequent recollection of the things that they say and do, and this is of particular importance in connection with the early postoperative management of ambulatory cases. Even under the best conditions, that is in patients below 60 years of age who have received only a sleep dose of thiopentone followed by nitrous oxide and oxygen, who have been lightly premedicated and who are

regarded as awake on leaving the operating theatre, only 40 per cent have well-ordered memories from the time of their return to bed.

From the point of view of the anaesthetist's responsibility for the patient, it is not sufficient merely to elicit some sign of wakefulness at the end of the operation. However "nontoxic" the anaesthetic agent, and however low its concentration, it must be remembered that the full restoration of normal activity in the central nervous system is by no means instantaneous.

SUMMARY

Patients were interviewed postoperatively and asked how soon they awoke from their anaesthetics. By selecting patients who were stated by the anaesthetist to be awake on leaving the operating theatre, it was possible to assess the duration of postoperative amnesia and to study the influence of some modifying factors.

Patients over the age of 60 showed an increasing tendency to be unaware of their actual time of awaking. Postoperative amnesia of more than 8 hours duration was common in old people.

The use of hyoscine in premedication led to a significant prolongation of postoperative amnesia.

In comparison with nitrous oxide and oxygen anaesthesia, equipotent ether-air mixtures produced greater degrees of postoperative amnesia, even when the patient was awake at the conclusion of surgery, and trichloroethylene-air mixtures produced very marked amnesia which occasionally lasted for days.

Patients operated on during the first 12 hours of the day tended to have rather longer periods of amnesia than those operated on during the second half of the day. However, most of the old patients in the series were operated on during the first half of the day.

When postoperative drugs were administered during the amnesic period, the return of memory was significantly delayed.

Even under the most favourable conditions, only approximately 40 per cent of patients had clear and continuous memories from the time of their return to bed.

REFERENCE

Artusio, J. F. (1955). Ether analgesia during major surgery. *J. Amer. med. Ass.*, **157**, 33.

Brit. J. Anaesth. (1961), 33, 405

ABNORMAL RESPONSE TO SUXAMETHONIUM IN POLYARTERITIS NODOSA

BY

M. W. POTTS AND J. A. THORNTON

*Department of Anaesthetics, Guy's Hospital, London, S.E.*1

POLYARTERITIS NODOSA is a disease in which widespread acute necrosis occurs in the arteries, leading to a variety of functional disturbances involving the nervous system, heart, kidneys, lungs, abdominal viscera, and blood (Harvey, 1959). The liver is affected in this condition more frequently than is recognized. The following case report illustrates the need for care in the administration of muscle relaxants to patients suffering from polyarteritis nodosa.

CASE REPORT

A male, J. W., aged 60, occupation a railway checker, was admitted to hospital on August 6, 1960, complaining of swelling and pain in the hands, with blueness of the tips of the fingers for two weeks. There was nothing of relevance with respect to personal history, family history or previous diseases. Three to four months before admission he began to get aching pains in both hips and was told that it was lumbago. This pain recurred on and off for about two months. Five weeks prior to admission pain began in his calves which did not get better with rest and he was referred for physiotherapy. However, he did not improve with treatment and three weeks later his fingers began to swell and the nail beds went blue: this was followed a few days later by swelling of the backs of the hands and the cyanosis spread to involve the distal phalanges.

Examination on admission revealed auricular fibrillation. Peripheral pulses were present and the blood pressure was 210/100 mm Hg. He was moderately emphysematous. Examination of the hands revealed swollen index, middle, and little fingers of both hands. The terminal phalanges were blue. Examination of the heart and abdomen revealed no abnormality. A provisional diagnosis of polyarteritis nodosa was made.

He was treated with tolazoline and achromycin initially and 11 days later he was given prednisolone. Nevertheless 16 days after admission the blueness had extended, accompanied by blistering; at this stage heparin therapy was started. The next day he had developed a nodular lesion on his right buttock and an area of blueness on the dorsum of his right foot. As a result of the latter it was decided that a retrograde aortogram should be carried out.

Investigation up to this time had revealed a raised E.S.R. (75 mm 1st hour), fasting blood sugar of 89 mg/100 ml; plasma uric acid 4.3 mg/100 ml; urine no abnormal constituents; serum cholesterol 220 mg/100 ml; cold agglutinins nil; Hb 80 per cent; total proteins 6.4 gm/100 ml. Electrophoresis showed a reduced albumin and a slightly raised alpha-2 globulin with no abnormal fractions. There was no eosinophilia.

Retrograde aortogram and biopsy of skin. Premedication consisted of pethidine 50 mg and atropine 0.6 m.g. i.m. 1 hour before induction of anaesthesia. The latter was carried out with a cyclopropane and oxygen mixture in a closed circuit. When adequate relaxation had been achieved following the administration of 25 mg of suxamethonium chloride an armoured No. 10 latex tube was passed, after topical anaesthesia of the cords had been induced with 4 per cent lignocaine. Ventilation was maintained with 75 per cent nitrous oxide and 25 per cent oxygen. Spontaneous respiration did not return until 40 minutes after the administration of suxamethonium. Subsequently anaesthesia was maintained with nitrous oxide, oxygen and halothane. This was discontinued 1 hour after induction, on completion of the investigation.

Recovery was normal and there was no postoperative respiratory insufficiency. Some hours after the aortogram, it was noticed that pulses were absent in the right leg and a diagnosis of femoral artery thrombosis was therefore made; it was decided that thromboendarterectomy was necessary.

For his second anaesthetic premedication consisted of pethidine 50 mg and atropine 0.6 mg and anaesthesia was induced with thiopentone 150 mg and suxamethonium 25 mg. (Owing to an unfortunate series of circumstances no record of the previous abnormal reaction to the relaxant drug was available to the anaesthetist on this second occasion). After intubation with a No. 10 cuffed endotracheal tube, the lungs were rhythmically inflated with a nitrous oxide and oxygen mixture and, as before, spontaneous ventilation did not return until 40 minutes after the administration of the suxamethonium; at this time the skin was being sutured. The patient was returned to the ward and postoperative recovery was uneventful.

The second anaesthetist subsequently ascertained that prolonged apnoea had occurred after the previous administration of suxamethonium and it was therefore decided to estimate the serum cholinesterase content. This was done 2 days later and found to be 7μlCO_2/ml/min. As a result the liver function was tested and the results were as follows:

Direct Van den Bergh	Negative
Serum bilirubin	0.4 mg/100 ml
Zinc turbidity	3 units
Thymol turbidity	2 units
Thymol flocculation	Negative
Colloidal gold	Negative
Albumin	2 g/100 ml
Globulin	4.2 g/100 ml
Total protein	6.2 g/100 ml
A/G ratio	0.5/1
Alkaline phosphatase	32.3 K.A. units/100 ml*

*The normal range for serum cholinesterase is 53–102 μlCO_2/ml/min with a mean value of 76μl (Thompson and Trounce, 1956).

Histological examination of the skin biopsy confirmed the provisional diagnosis of polyarteritis nodosa.

Subsequent repeat liver function tests showed a gradual return to normal and four months later the cholinesterase level was found to be 44μl CO_2/ml/min with an E.S.R. of 21 mm 1st hour. There had been no further progress of the disease process as evidenced by the lesions of the extremities.

DISCUSSION

An association has previously been noticed between certain of the so-called "collagenoses" and the myasthenic state: the diseases referred to are polymyositis, dermatomyositis, and systemic lupus erythematosus; the muscle weakness has responded to neostigmine (Rees and Harman, 1950; Bonduelle, Bouygues and Coulon, 1955).

Commenting on the anaesthetic technique in such myasthenic states, McClelland (1960) has pointed out that the use of muscle relaxants is contraindicated by an abnormal response of the neuromuscular junction.

Further, it has been noted that significant liver dysfunction can occur in polyarteritis nodosa (Rose and Spencer, 1957) and to this must be added lupus erythematosus (Jessar, Lamont-Havers and Ragan, 1953). In these illnesses there is often surprisingly little clinical evidence to suggest liver dysfunction. However, Jessar and his colleagues found that of 15 autopsy examinations in lupus erythematosus, 4 had hepatic lesions; whilst Harvey and his co-workers (1954) found 40 cases of hepatic involvement out of a total of 84 autopsies in cases of polyarteritis nodosa.

A low cholinesterase level is a recognized feature of impaired liver function (McArdle, 1940).

The presence of either of the latter two of this loosely associated group of diseases thus furnishes a further possible contraindication to the use of a muscle relaxant, in this case suxamethonium; should general anaesthesia become necessary.

It will also be recalled that Dundee and Gray (1953) focused attention upon the observation that patients with liver dysfunction were more resistant to d-tubocurarine than normal healthy subjects. They suggested, in explanation, an association with the pseudocholinesterase level, which if low might reasonably be reflected in a higher than normal concentration of acetylcholine at the motor endplate requiring more d-tubocurarine than usual to produce paralysis.

There thus appears to be an indication to use d-tubocurarine rather than suxamethonium in the presence of polyarteritis nodosa or lupus erythematosus. However, in one of the above-mentioned diseases, lupus erythematosus, there are reports of both a myasthenic state and significant liver dysfunction.

There is no evidence to suggest that these abnormalities were co-existent: nevertheless it seems safest to avoid, or use with great caution, any muscle relaxant, depolarizing or nondepolarizing, in such circumstances until one is in a position to rule out the possibility of a myasthenic state on the one hand, or liver dysfunction on the other.

This case report underlines three important factors. Firstly that impaired liver function may be an unrecognized feature of polyarteritis nodosa in the absence of clinical signs, and secondly that liver involvement is not an infrequent occurrence. Thirdly it stresses the importance of adequate, readily available, anaesthetic records and emphasizes the desirability of a pre-anaesthetic serum cholinesterase estimation in this disease (particularly during an exacerbation) if the use of suxamethonium is contemplated.

SUMMARY

Prolonged apnoea occurred following suxamethonium administration to a patient suffering from polyarteritis nodosa.

The relationship between some of the "collagenoses" and significant liver dysfunction is discussed.

It is concluded that all muscle relaxants should be avoided or used with extreme caution, in the presence of polymyositis, dermatomyositis, systemic lupus erythematosus and polyarteritis nodosa, unless prior investigations of hepatic function have been found to be normal.

REFERENCES

Bonduelle, M., Bouygues, P., and Coulon, J. (1955). Le syndrome myasthenique de polymosites. *Rev. neurol.*, **92**, 546.

Dundee, J. W., and Gray, T. C. (1953). Resistance to d-tubocurarine chloride in the presence of liver damage. *Lancet*, **2**, 16.

Harvey, A. M., Tumulty, P. A., Shulman, L. E., Conley, C. L., and Shoenvich, E. H. (1954). Systemic lupus erythematosus: Review of the literature and clinical analysis of 138 cases. *Medicine (Baltimore)*, **33**, 291.

Harvey, A. Mc.G. (1959), in *Textbook of Medicine* (10th ed.), edited by Cecil, R. L., and Loeb, R. F., vol. 1, p. 467. Philadelphia and London: Saunders.

Jessar, R. A., Lamont-Havers, W., and Ragan, C. (1953). Natural history of lupus erythematosus disseminatus. *Ann. intern. Med.*, **38**, 171.

McArdle, B. (1940). The serum cholinesterase in jaundice and diseases of the liver. *Quart. J. Med.*, **9**, 107.

McClelland, R. M. A. (1960). Myasthenic state and myotonic syndrome. *Brit. J. Anaesth.*, **32**, 81.

Rees, H., and Harman, J. W. (1954). Hitherto unclassified muscular disorder. *Trans. Amer. neurol. Ass.*, **79**, 82.

Rose, G. A., and Spencer, H. (1957). Polyarteritis nodosa. *Quart. J. Med.*, **26**, 43.

Thompson, R. H. S., and Trounce, J. R. (1956). Serum cholinesterase levels in diabetes mellitus. *Lancet*, **1**, 656.

BOOK REVIEW

Principles of General Neurophysiology Relating to Anaesthesia and Surgery. By Barry Wyke. Published by Butterworth & Co., London. Pp. 136. Price 21*s*. net.

This book, which, as the Preface says, is a reprint with minor modifications, of Chapter V, Vol. I, of *General Anaesthesia*, edited by Frankis T. Evans and Cecil Gray, is designed for anaesthetists and surgeons who require information on the basic aspects of general neurophysiology. There have been so many recent advances in neurophysiology of particular importance to anaesthetists that a book of this sort should be especially welcome. Perhaps the most important to anaesthetists of all recent experiments are those relating to the mechanisms for consciousness and unconsciousness. The fundamental experiment that changed all previously held ideas about consciousness was that performed by Moruzzi and Magoun in 1949. They showed that repetitive stimulation of the reticular formation in the brain stem induced e.e.g. arousal. The extent of the control exercised by the reticular system on other brain mechanisms has yet to be defined but appears to be very wide indeed. Other recent experiments have shown that the reticular system itself is under the control of other brain mechanisms, particularly cortical. In fact we are beginning to realize that it is the brain as a whole that must be studied rather than its individual components. It is very disappointing, therefore, to find that all this work remains almost unmentioned in this book. The first half deals very adequately with the physiology and pharmacology of neurones and the physiology of synaptic transmission. The latter half of the book deals with cerebral circulation and metabolism and the physiology of the cerebro-spinal fluid. All this is well done and covers important subjects, particularly the effects of hypothermia. There are, however, only some twenty pages in the middle of the book, entitled "Electrical activity of the brain", which cover electroencephalography and touch lightly on the neurological basis of general anaesthesia. The section on electroencephalography is very much simplified, perhaps over much, since no mention is made of the great individual differences that exist from person to person. For example, it is suggested that everybody has an alpha rhythm which is responsive to opening and shutting the eyes. In fact, only about two-thirds of the population have this type of rhythm. The possible function of the alpha rhythm is not discussed at all, and the great dissociation that often exists between behaviour and the electroencephalogram is not mentioned. Perhaps the most striking example of this is the action of atropine on the dog. Under the influence of this drug the animal is obviously alert and wide awake, yet the electroencephalogram is like that of a sleepy animal. The effects of hyperventilation also are very variable. There is a section on the electroencephalographic monitoring of anaesthesia in which it is suggested that the electroencephalograph will always give a precise and accurate indication of the depth of anaesthesia in any particular subject. Recent experiments have suggested that this is by no means always so. In a mere two pages, entitled "A neurological basis for general anaesthesia", is considered, or rather, left unconsidered, the workings of the reticular system and the whole problem of the mechanisms for consciousness and unconsciousness. In the introduction to this book Dr. Wyke says that no reference is made to the special physiology of the sensory, motor or visceral nervous system. In the only mention of pain in the book, and surely pain is important to anaesthetists and surgeons alike, Dr. Wyke says that "it is important for the anaesthetist to realize that even in a deeply anaesthetized patient volleys of impulses from peripheral sensory receptors, especially pain receptors, continue to bombard the sensory sectors of the cerebral cortex through the thalamo-cortical relays thereto". Recent work makes it almost certain that there is no lemniscal pathway for pain, and that painful stimuli travel up the cortex only via the secondary extralemniscal pathways. These secondary pathways are particularly susceptible to anaesthetic agents, and it is practically certain that no painful stimuli reach the cortex during very light anaesthesia.

On the whole this book appears to follow the classical approach to neurophysiology in that it considers the workings of individual units rather than the workings of the brain as a whole, and it is becoming clear that it is the working of the brain as a whole that is of particular importance to anaesthetists.

There is a table of contents designed to guide the reader to any particular section of the book, but surely if a book of this sort is worth reading it is worthy of an index? *J. Clutton-Brock*

Brit. J. Anaesth. (1961), 33, 408

A METHOD OF ANAESTHESIA FOR CAESAREAN SECTION

Evolution of a technique suitable for use in a country hospital

BY

C. A. G. ARMSTRONG

Mid-Ulster Hospital, Magherafelt, Co. Londonderry, Northern Ireland

THE practice of modern obstetrics has reached a high level of efficiency and requires equally efficient anaesthesia. Caesarean section is often performed to increase the baby's chance of survival and the anaesthetic should not appreciably decrease this chance. A maternal death due to anaesthesia is an unacceptable tragedy. Since there is no generally accepted "best" method of anaesthesia for this common operation, it may be of value to record an individual attempt made by the author, working single-handed in a country hospital, to devise a technique suitable for both mother and baby. The following observations are offered for the consideration of anaesthetists who may find themselves working in similar circumstances.

The two most important considerations in the design of a suitable technique are to reduce (1) the risk of maternal vomiting and (2) the effects of the anaesthetic on the foetus. In addition, however, several possible complicating factors may arise. For example, the patient may be toxaemic, shocked, or exhausted by a long unsuccessful labour. Sometimes, too, uterine relaxation may be necessary. Or again, for obstetric reasons, the operation may have to be performed speedily. Finally the obstetrician may use drugs which influence or limit the choice of agents available to the anaesthetist.

Most patients in this country prefer to be unconscious during the operation of Caesarean section so that, while many advantages have been claimed for conduction techniques, only general anaesthesia will be discussed here. It is widely accepted that a skilled and experienced anaesthetist should be available for every obstetric anaesthetic, and in considering technique this is presumed to be the case.

VOMITING

In the past few years the increased awareness, largely due to the activities of the Committee of the Association of Anaesthetists on deaths under anaesthesia (Morton and Wylie, 1951) and the writings of Parker (1954), of the danger of vomiting during obstetrical anaesthesia has apparently reduced the maternal mortality from this cause, though fatalities still occur (Walker et al., 1960).

Various well recognized precautions have been advocated to diminish the risk of vomiting and subsequent aspiration. It seems, however, to be difficult or impossible to predict which obstetric patients are most likely to vomit. Therefore, if it is desired to ensure that the stomach shall be empty in all cases every patient must be subjected to pre-operative treatment to this end, and most obstetricians will protest if their patients are submitted routinely to procedures so uncomfortable or dangerous as gastric intubation or apomorphine administration. It would be easier to argue against such protests if these harsh measures invariably prevented vomiting during anaesthesia, but they do not. Therefore the anaesthetist should aim at a technique unlikely to cause vomiting or regurgitation during induction and one which prevents the aspiration of vomit for the remainder of the anaesthetic.

The trend of present opinion seems to favour induction with thiopentone and a relaxant followed by the passage of a cuffed endotracheal tube. Bourne (1956), however, prefers to use an inhalation agent instead of thiopentone in this sequence.

The chance of regurgitation of stomach contents following relaxant administration may be diminished by having the patient steeply tilted foot down during induction (Snow and Nunn, 1959). When the endotracheal tube is in place with the cuff inflated, complete security against aspiration has been achieved and maintenance of anaesthesia by any agent is made easy. Routine use of a cuffed endotracheal tube for Caesarean

anaesthesia has been strongly advocated by a number of writers (Armstrong, 1956; Coleman and Day, 1956; Bingham, 1957; Hodges et al., 1959a). A powerful argument for simpler methods has, however, been advanced by Dinnick (1957) who supports his view by the fact that in the Middlesex Hospital there has been no death from inhalation of vomit in the maternity department for a period of twenty-five years during which these simpler methods were in use. In spite of this fine record there is no doubt that opinion is moving towards routine intubation, and this is reflected in the "Report on Confidential Enquiries into Maternal Deaths 1955–1957" (Walker et al., 1960). This states: "It is striking that in ten cases, including three Caesarean sections, tracheal intubation does not appear to have been planned. Although in seven cases vomiting occurred before intubation could be completed, it is likely that more widespread use of tracheal intubation has avoided many fatalities from this cause."

Whatever method is to be employed the anaesthetist should be on the alert for vomiting, should use a tilting table, and have available an efficient suction apparatus and a bronchoscope.

EFFECT ON THE FOETUS

Some anaesthetic drugs given to the mother pass into the foetal circulation and may delay the onset of respiration in the newborn infant. This is generally assumed to be a harmful effect but it could be advantageous if the infant's first breath were delayed just long enough to allow the pharynx to be cleared of liquor, whose inhalation by an active baby is a danger in abdominal delivery. Anaesthetic depression is not the only factor which may delay neonatal respiration, though others have not yet been very clearly defined. James (1960) mentions biochemical changes and birth trauma, while Hodges and his colleagues (1960a) regard pre-operative foetal distress, pre-operative administration of sedative drugs to the mother, and a prolonged interval (associated with obstetric difficulties) between induction of anaesthesia and delivery as the main nonanaesthetic causes of delayed respiration in the baby. Because of the existence and the indeterminate nature of these additional factors the clinician naturally finds it difficult to discover a regular correlation between depth of maternal anaesthesia and recovery time of the baby. It is therefore surprising to read of a recent series of operative deliveries in which all the babies cried within 2 minutes of delivery (Kane and Stephens, 1959). It is impossible deliberately to use the anaesthetic to produce just enough delay in onset of respiration to ensure that the baby's first breath will not occur until the head has been delivered, but it should be possible to design for the mother an anaesthetic technique which has a negligible effect on the baby's recovery, and this should be the aim of the anaesthetist. The problem of inhalation of liquor must be solved in some other way.

OTHER FACTORS

Usually uterine relaxation is neither necessary nor desirable in Caesarean section but occasionally it may be a great help to the obstetrician. To achieve it, the chosen anaesthetic technique should be capable of modification by the addition of halothane or ether. A relaxed uterus, however, will then be attained only at the price of some depression of the baby.

Exhausted or shocked patients require suitable reduction in dose of the agents used and in very severe shock some anaesthetists prefer to avoid thiopentone. It is the author's experience that severe pre-eclamptic toxaemia seems to make the patient unusually intolerant of blood loss and it is wise to be fully prepared to give a blood transfusion to toxaemic patients.

Oxytocin may be used by the obstetrician to induce labour or to cause contraction of the uterus after delivery. Lesser and Eason (1954) have reported a death from ventricular fibrillation following the combination of oxytocin and cyclopropane, which should therefore be avoided when oxytocin is used. Hodges and his co-workers (1959b) have observed that intravenous infusion of oxytocin may modify the action of suxamethonium so that the normal depolarizing effect is replaced by neuromuscular block of a nondepolarizing type. They suggest that it is reasonable to expect that oxytocin might cause an increased susceptibility to a nondepolarizing relaxant such as tubocurarine, although they have no clinical evidence that this is so. At this stage it can only be said that when an oxytocin drip precedes Caesarean section the

anaesthetist should beware of abnormal reactions to any of the relaxant drugs.

CHOICE OF DRUGS

Thiopentone might be considered an unpromising drug for obstetric anaesthesia because it is a respiratory depressant which crosses the placental barrier. Formerly it was held that the placenta delayed maximum transmission of barbiturates for at least 5 minutes (Dundee, 1956), but it now appears that this is not so (Dundee, 1959). According to Crawford (1959a), when thiopentone is given to the mother the level of the drug in the foetal circulation quickly equals that in the maternal circulation and thereafter both fall in an exponential manner. Presumably, if the single induction dose of thiopentone is kept sufficiently small, and if the interval between its injection and delivery of the baby is long enough, then the level in the foetal blood will be so low that it will not cause any appreciable depression of respiration. Opinions vary regarding the permissible size of the induction dose, quantities ranging from 200 mg (Hodges et al., 1959a) to 300 mg (Crawford, 1959b) being mentioned. There is no general agreement on the relationship between thiopentone and the vomiting risk. On one hand, it is claimed that the risk of vomiting is decreased by the tranquil induction usual with thiopentone. On the other hand, the danger of sudden massive regurgitation following thiopentone is stressed.

Nitrous oxide, with at least 20 per cent oxygen, given to the mother appears to cause no delay in the onset of neonatal respiration.

Placental transmission of cyclopropane does take place but the rate of transmission is uncertain (Crawford, 1959c). Apgar and her colleagues (1957) have drawn attention to adverse effects on the baby following its use. Cyclopropane has enjoyed popularity in obstetric anaesthesia because it is a rapidly acting and readily controllable agent which can be given with a high percentage of oxygen. In addition to the harmful effects upon the foetus, it has the disadvantages of being incompatible with oxytocin, and of being liable to cause cardiac arrythmias and occasionally laryngeal spasm.

The outstanding property of halothane in obstetrics is its ability to cause uterine relaxation (Embrey, Garrett and Pryer, 1958). This takes place quickly and in a relatively light plane of anaesthesia, so that halothane may be of great value when the obstetrician requires a relaxed uterus. Halothane is unsuitable when this effect is unwanted. The use of halothane as the main anaesthetic agent in a small series of Caesarean sections, apparently with satisfactory results, has been reported (Brown and Woods, 1958) but few would agree with these authors that "uterine contraction and retraction are not affected".

Diethyl ether is a less suitable agent if a tranquil induction is wanted. The drug is transmitted across the placenta (Lee, 1959) but, as it is not a powerful respiratory depressant, light maternal anaesthesia with ether should not cause undue delay in respiration of the newborn baby. The uterus can be relaxed, but the depth of ether anaesthesia required to do this may take 15 or 20 minutes to attain.

Hydroxydione produces a remarkably tranquil induction, and its use for Caesarean section has been advocated by Galley and Lerman (1959). It is thought to be a promising agent in obstetric anaesthesia (Ransom, 1959).

Of the commonly used relaxants, gallamine is the only one which has been shown to pass the placenta in amounts which might be harmful to the foetus (Crawford, 1956). Suxamethonium (Wylie and Churchill-Davidson, 1960) and d-tubocurarine (Gray, 1947; Crawford, 1956) do not appear to reach the foetal circulation and can be used freely without fear of causing apnoea neonatorum. It may be that the danger of regurgitation of stomach contents is slightly increased by the period of muscle twitching which often follows suxamethonium administration.

EVOLUTION OF PRESENT METHOD

In 1957 the author believed that his standard of anaesthesia for Caesarean section could be improved by applying the methods of induction then in use for general abdominal surgery. The technique chosen was as follows:

> Anaesthesia was induced with a full dose of thiopentone (400 to 500 mg) and was followed by a relaxant (gallamine 80 mg or tubocurarine 15 mg or suxamethonium 50 mg). After a short period of inflation of the lungs with oxygen, endotracheal intubation was carried out with a cuffed tube and thereafter anaesthesia was maintained using cyclopropane and oxygen in a closed circuit. Anaesthesia was induced on the operating table; an electrical suction

apparatus was tested and kept running. If vomiting occurred before intubation, the table was tilted steeply head down and the pharynx promptly cleared by suction. No special effort was made to minimize the time between induction of anaesthesia and delivery of the baby.

A record was kept of each anaesthetic, and the intervals between induction and delivery and between delivery and onset of continuing respiration of the baby were timed. The latter interval was chosen because, as Ozinsky and Harrison (1956) have pointed out, it gives a more accurate indication of the state of the baby than "breathing time" or "crying time".

Forty patients undergoing Caesarean section were anaesthetized in this way. Of these, two mothers vomited between induction and intubation but fortunately aspiration was avoided and the patients suffered no sequelae.

Of the forty babies, only ten were breathing satisfactorily within 2 minutes of birth, and the average time between delivery and continuing respiration was 5.4 minutes. No correlation could be found between the induction to delivery interval and the speed of recovery of the baby. The undue depression of the babies in the group was attributed to the overgenerous induction dose of thiopentone. The dose was therefore reduced to a maximum of 250 mg for the next group of fifty Caesarean sections, the technique being otherwise unchanged. Of these patients, one mother vomited between induction and intubation, without aspiration or other sequelae.

Of the fifty babies, satisfactory respiration was established in twenty-six within 2 minutes of birth, and the average time between delivery and continuing respiration was 3.5 minutes. While this represented a decided improvement on the previous group, it seemed that the anaesthetic still delayed unduly the onset of respiration in many babies. Another rather serious disadvantage of this technique was that such dosage of thiopentone and relaxant gave far from ideal conditions for intubation. A struggle to intubate is dangerous to the patient and humiliating for the anaesthetist.

Since, according to Apgar and her colleagues (1957), cyclopropane given to the mother has an adverse effect on the recovery of the baby, it was decided to exclude this agent from the next technique to be used, which was as follows:

The patient, premedicated with atropine 0.6 mg. is placed on the operating table which is tilted steeply foot down (Snow and Nunn, 1959). The suction apparatus is tested and kept running. Through a Gordh needle a test dose of d-tubocurarine 5 mg is injected intravenously (Gray, 1959). If there is no abnormal reaction, thiopentone 100 mg in 2½ per cent solution is injected, followed immediately by d-tubocurarine 25 mg. After a short pause a further dose of 150 mg of thiopentone is added. It is felt that this sequence of injection allows the relaxant to develop most of its effect before that of the thiopentone wears off. A short period of gentle inflation of the lungs with nitrous oxide and oxygen is carried out and when the jaw is relaxed a cuffed endotracheal tube is introduced. The patient is then hyperventilated with a mixture of 80 per cent nitrous oxide and 20 per cent oxygen, following the technique of Geddes and Gray (1959). On delivery of the baby, ergometrine maleate 0.5 mg is given through the Gordh needle and the obstetrician places the baby on a table where there is a pillow covered by a sterile towel, allowing a head-down tilt. The anaesthetist clears the baby's pharynx by mechanical suction and, assisted by the midwife, carries out whatever resuscitation is thought necessary. This arrangement allows endotracheal intubation of the baby to be carried out quickly if it is considered advisable. The author agrees with the view of Hodges and his colleagues (1960b) that endotracheal intubation and inflation with oxygen is the most effective means available of resuscitating the newborn, and should be used earlier and more frequently than is common practice. Almost certainly this valuable measure was foolishly delayed or denied to many asphyxiated babies in this series.

At the end of operation atropine and neostigmine are given if the mother still shows signs of curarization.

Thirty patients undergoing Caesarean section were anaesthetized by the above technique. In the first fifteen cases in this group three babies gasped and inhaled liquor during delivery with consequent delay in establishing respiration. Therefore in the later cases the obstetrician's assistant cleared the baby's pharynx by suction during delivery.

Two modifications of the technique might be necessary in certain circumstances, which did not in fact arise in any of the thirty cases recorded. First there are instances where an examination under anaesthesia is necessary to decide whether or not to proceed with Caesarean section. In these, suxamethonium should be substituted for d-tubocurarine which is given later if necessary. Second, the obstetrician may request uterine relaxation. Here halothane vapour should be added to the gas mixture for a few minutes before the uterus is opened, a most careful watch being kept on the maternal blood pressure during the halothane administration.

COMPARISON OF RESULTS

Records were kept during the three stages of development of the anaesthetic technique, and the results are grouped as follows:

Group I. Induction with thiopentone 400 to 500 mg, relaxant (tubocurarine 15 mg or gallamine 80 mg or suxamethonium 50 mg), and maintenance with cyclopropane and oxygen.

Group II. Induction with not more than 250 mg of thiopentone, relaxant (tubocurarine 15 mg or suxamethonium 50 mg), and maintenance with cyclopropane and oxygen.

Group III. Induction with not more than 250 mg thiopentone, relaxant (tubocurarine 30 mg), and maintenance with a nitrous oxide and oxygen mixture.

The results are summarized in table I, and the

histograms (fig. 1) compare the recovery times of the babies in the three groups. It is evident that each successive change in technique brought an improvement in the state of the babies. While 30 per cent of the babies in group I were severely depressed, it must be remembered that the end-point of continuing respiration was not recorded until the baby's respiration was fully established, and before this point was reached intermittent breathing took place. None of the babies in any group failed to establish respiration.

Slightly more than half of the babies in group II were considered satisfactory, and here it is felt that cyclopropane was an important factor causing neonatal depression. Its exclusion led to a marked improvement in group III. While the results seem to indicate that the technique used in group III is an acceptable one, the ideal of negligible anaesthetic depression of the baby has not yet been reached.

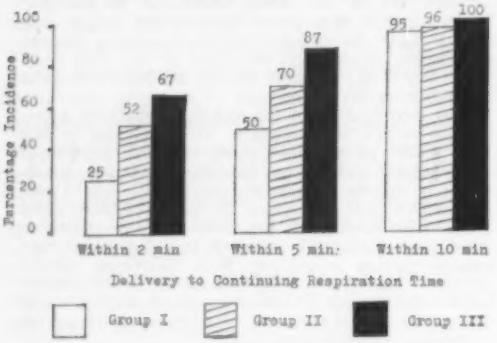


FIG. 1

The percentage of babies who established continuing respiration within 2, 5, and 10 minutes of delivery in three groups in which differing anaesthetic methods (described in the text) were used.

Finally, no correlation could be found between the induction-to-delivery interval and the speed of recovery of the baby in any group, nor in the results of the three groups taken together.

DISCUSSION

In this series of cases no account has been taken of the nonanaesthetic factors, such as pre-operative foetal distress, which are known to lead to neotal depression.

While no firm conclusions may be based on such a small series, the results obtained indicate that techniques using thiopentone for induction and cyclopropane for maintenance are unsuitable for Caesarean section because of the depressant effect on the babies. A technique consisting of a limited dose of thiopentone for induction, a muscle relaxant, and nitrous oxide and oxygen for maintenance, is acceptable but not ideal.

A routine assessment of the state of the baby delivered by Caesarean section is almost certainly valuable to indicate the success (or otherwise) of the anaesthetic technique used. The baby's condition can be simply gauged by recording the time between delivery and onset of continuing respiration, or by scoring on the Apgar system (Apgar, 1953). A healthy dissatisfaction with the anaesthetic method may result.

SUMMARY AND CONCLUSIONS

The requirements of anaesthesia for Caesarean section are discussed.

TABLE I

Results obtained in three groups of patients undergoing Caesarean section

	Group		
	I (40 patients)	II (50 patients)	III (30 patients)
Average interval between delivery and continuing respiration (min)	5.4	3.5	1.8
Satisfactory babies (delivery to continuing respiration interval not over 2 minutes)	10 (25%)	26 (52%)	20 (67%)
Severe neonatal asphyxia (delivery to continuing respiration time 8 or more minutes)	12 (30%)	6 (12%)	1 (3.3%)
Mother vomited	2 (5%)	1 (2%)	1 (3.3%)
Baby inhaled liquor	1 (2.5%)	3 (6%)	4 (13.3%)

Following a decision to apply the induction methods in use for general surgery to Caesarean section, an anaesthetic technique was used which consisted of a large induction dose of thiopentone, a relaxant, endotracheal intubation and maintenance by cyclopropane. Recordings of the time between delivery and onset of continuing respiration of the baby revealed that this technique produced severe depression in many babies. Reduction of the dose of thiopentone led to an improvement. When, in addition, nitrous oxide was substituted for cyclopropane, a further improvement resulted. It was concluded that large induction doses of thiopentone and cyclopropane should both be avoided in Caesarean anaesthesia because of their effects on the baby.

An opinion was expressed that routine assessment of the baby delivered by Caesarean section is a valuable indication of the success of the anaesthetic technique used.

ACKNOWLEDGMENTS

I should like to express my gratitude to Mr. John Watson, whose patients formed this series, for his sustained interest and co-operation; and to Dr. J. W. Dundee for help and encouragement in the preparation of the paper. My thanks are also due to Mr. H. W. Young, who read the original typescript and amended many errors of grammar and style.

REFERENCES

Apgar, V. (1953). Proposal for a new method of evaluation of the newborn infant. *Curr. Res. Anesth. Analg.*, **32**, 260.

—— Holaday, D. A., James, L. S., Prince, C. E., and Weisbrot, I. M. (1957). Comparison of regional and general anesthesia in obstetrics: with special reference to the transmission of cyclopropane across the placenta. *J. Amer. med. Ass.*, **165**, 2155.

Armstrong, C. A. G. (1956). Anaesthesia and apnoea neonatorum after Caesarean section. *Brit. med. J.*, **1**, 860.

Bingham, W. (1957). Balanced anaesthesia for Caesarean section. *Anaesthesia*, **12**, 435.

Bourne, J. G. (1956). Anaesthesia and apnoea neonatorum after Caesarean section. *Brit. Med. J.*, **1**, 984.

Brown, T. A., and Woods, M. A. (1958). Halothane in a country hospital. *Brit. J. Anaesth.*, **30**, 333.

Coleman, D. J., and Day, B. L. (1956). Anaesthesia for operative obstetrics. *Lancet*, **1**, 709.

Crawford, J. S. (1956). Some aspects of obstetric anaesthesia. *Brit. J. Anaesth.*, **28**, 146.

—— (1959a). *Principles and practice of obstetric anaesthesia* (1st ed.), p. 27. Oxford: Blackwell.

—— (1959b). Ibid., p. 61.

—— (1959c). Ibid., p. 24.

Dinnick, O. P. (1957). Discussion on anaesthesia for obstetrics: an evaluation of general and regional methods. *Proc. roy. Soc. Med.*, **52**, 547.

Dundee, J. W. (1956). *Thiopentone and other thiobarbiturates* (1st ed.), p. 91. Edinburgh: Livingstone.

—— (1959), in *General Anaesthesia* (1st ed.), edited by Evans, F. T., and Gray, T. C., vol. I, ch. 2, p. 356. London: Butterworth.

Embrey, M. P., Garrett, W. J., and Pryer, D. L. (1958). Inhibitory action of halothane on contractility of human pregnant uterus. *Lancet*, **2**, 1093.

Galley, A. H., and Lerman, L. H. (1959). New technique with hydroxydione. *Brit. med. J.*, **1**, 332.

Geddes, I. C., and Gray, T. C. (1959). Hyperventilation for the maintenance of anaesthesia. *Lancet*, **2**, 4.

Gray, T. C. (1947). d-Tubocurarine in Caesarean section. *Brit. med. J.*, **1**, 444.

—— (1959), in *General Anaesthesia* (1st ed.), edited by Evans, F. T., and Gray, T. C., ch. 14, p. 433. London: Butterworth.

Hodges, R. J. H., Bennett, J. R., Tunstall, M. E., and Knight, R. F. (1959a). General anaesthesia for operative obstetrics, with special reference to the use of thiopentone and suxamethonium. *Brit. J. Anaesth.*, **31**, 152.

—— —— —— Shanks, R. O. F. (1959b). Effects of oxytocin on the response to suxamethonium. *Brit. med. J.*, **1**, 413.

—— Tunstall, M. E., Knight, R. F., and Wilson, E. J. (1960a). Some factors associated with neonatal depression in operative obstetrics. *Brit. J. Anaesth.*, **32**, 16.

—— —— (1960b). Endotracheal aspiration and oxygenation in resuscitation of the newborn. *Brit. J. Anaesth.*, **32**, 9.

James, L. S. (1960). The effect of pain relief for labor and delivery on the fetus and newborn. *Anesthesiology*, **21**, 405.

Kane, P. O., and Stephens, C. J. (1959). Buthalitone sodium: its effect on the foetus and its rate of passage across the human placenta. *Brit. J. Anaesth.*, **31**, 533.

Lee, J. A. (1959). *A Synopsis of Anaesthesia* (4th ed.), p. 94. Bristol: Wright.

Lesser, M., and Eason, G. A. (1954). Cardiac arrest under anaesthesia during induction of labour with "Pitocin" drip. *Brit. med. J.*, **2**, 79.

Morton, H. J. V., and Wylie, W. D. (1951). Anaesthetic deaths due to regurgitation or vomiting. *Anaesthesia*, **6**, 190.

Ozinsky, J., and Harrison, G. C. (1956). Effect of duration of anaesthesia on apnoea neonatorum after Caesarean section. *Brit. med. J.*, **1**, 725.

Parker, R. B. (1954). Risk from the aspiration of vomit during obstetric anaesthesia. *Brit. med. J.*, **2**, 16.

Ransom, Shila (1959), in *General Anaesthesia* (1st ed.), edited by Evans, F. T., and Gray, T. C., ch. 12, p. 229. London: Butterworth.

Snow, R. G., and Nunn, J. F. (1959). Induction of anaesthesia in the foot-down position for patients with a full stomach. *Brit. J. Anaesth.*, **31**, 493.

Walker, A. L., Wrigley, A. J., Organe, G. S. W., Chamberlain, R. N., and Martin, W. J. (1960). *Report on confidential enquiries into maternal deaths in England and Wales, 1955–1957*. No. 103. London: H.M. Stationery Office.

Wylie, W. D., and Churchill-Davidson, H. C. (1960). *A Practice of Anaesthesia* (1st ed.), ch. IX, p. 586. London: Lloyd-Luke.

Brit. J. Anaesth. (1961), 33, 414

THE ANALEPTIC ACTION OF PHENYL-PYRROLIDINO-PENTANE

BY

W. SNIPER

Stobhill General Hospital, Glasgow, Scotland

PHENYL-PYRROLIDINO-PENTANE (p.p.p.) is a synthetic papaverine derivative, the pharmacology of which was originally investigated by Kadatz and Potzsch (1957). Its primary actions in animals appeared to result in an increase of blood pressure and a respiratory stimulant effect, both the depth and rate of respiration being affected. In addition, it was observed that animals treated with this drug consumed a greater quantity of food than controls and appeared to exhibit increased wakefulness. Experimental observations in the human subject (Pabst, 1958) confirmed the respiratory stimulant effect of the drug and the observations of Kafer (1957) appeared to demonstrate a pressor action.

PRELIMINARY OBSERVATIONS

The author's previous work on postoperative hypotension (Sniper, 1960) led him to become interested in the use of p.p.p. as a pressor agent for postoperative use and an attempt was made to assess its value in this respect. The drug was made available in 2-ml ampoules each containing 10 mg and this dose was given intravenously to patients in whom the systolic blood pressure was markedly low following operation.

It soon became apparent, however, that although undoubtedly capable of raising the blood pressure the drug was less effective in this respect than other commonly used pressor agents such as methoxamine. In nine cases of postoperative hypotension repeated blood pressure readings were taken and in six there was a rise following the intravenous injection of 2 ml of p.p.p. but in no case did the blood pressure approach the preoperative level. In three cases no rise occurred and in two of these methoxamine was given, causing an immediate rise in blood pressure, thus suggesting that the vasomotor system was capable of responding to an adrenergic stimulus. At the same time, early experience with the new drug indicated that it was capable of producing very marked improvement in the depth of respiration with a rapid lightening of anaesthesia. These points are illustrated in the following case.

CASE 1. The patient, a man aged 81 years, had a prostatectomy under thiopentone, nitrous oxide, oxygen and halothane anaesthesia lasting 35 minutes. His pre-operative systolic blood pressure was 135 mm Hg. During operation this fell to 90 mm Hg and he was given 200 ml of 5 per cent dextrose solution and 1 litre of blood. Thereafter his blood pressure rose to 115 mm Hg systolic but on lowering his legs at the end of operation it fell to 70 mm Hg. An intravenous injection of 2 ml of p.p.p. was given. This resulted in an increase in the depth of respiration but there was no change in blood pressure. A few minutes later he was given atropine 0.6 mg, as it was thought that the fall in blood pressure might have been caused by a vagal reflex, but no rise occurred. He was then given methoxamine 20 mg which, in fact, was an overdose. His systolic blood pressure rose immediately to 190 mm Hg. It was concluded, therefore, that p.p.p. was more akin to nikethamide than to the pressor drugs and it was decided to pursue the investigation with a view to assessing the value of p.p.p. as an analeptic.

RESULTS

In all, forty cases were treated with the drug. They were unselected and included patients in a wide age range, from young adults to the very old. The surgical procedures for which anaesthesia was required included both intra- and extra-abdominal operations and ranged from uterine dilatation and curettage taking 5 minutes to a gastrectomy following haematemesis which lasted 2 hours. The drug was used in patients exhibiting different types of respiratory pattern at the end of operation, from Cheyne-Stokes respiration in one patient and carbon dioxide narcosis in another, to normal type of respiration following a herniorrhaphy. Neither the operation itself nor any other feature of the procedure appeared to have any bearing on the effect of p.p.p.; the only relevant factor was the postoperative respiratory pattern. The assessments

of respiratory depth and rhythm and the diagnosis of the cause of the upset in respiration where this was present were made on clinical grounds.

Nine patients were considered to have normal postoperative respiratory patterns. In only one of these, a woman who had a dilatation of the cervix and currettage of the uterus under thiopentone, nitrous oxide and oxygen anaesthesia lasting 15 minutes, did the injection of p.p.p. produce an augmentation of respiration. In the others the effect was equivocal.

Twenty-seven cases were considered to have central depression of respiration due to the anaesthetic or analgesic agents used. In those cases where a muscle relaxant was used, the effects of the relaxant had worn off or had been antagonized by atropine and neostigmine before p.p.p. was used. The action of p.p.p. can be illustrated by describing two typical cases in this series.

CASE 2. A man aged 65 had a transurethral prostatectomy under thiopentone, nitrous oxide, oxygen and halothane anaesthesia lasting 25 minutes. His preoperative blood pressure was 155/80 mm Hg. During operation the blood pressure fell to 110 mm Hg systolic. Five per cent dextrose solution 500 ml and blood 250 ml were given. On lowering the legs after operation the blood pressure fell to 60 mm Hg and respiration became sighing and irregular. A 2-ml dose of p.p.p. was given intravenously and respiration promptly improved, becoming deeper and regular, but there was no change in blood pressure. Five minutes later, however, systolic blood pressure had risen to 110 mm Hg.

It was noted in several other cases that when the blood pressure did rise following injection of p.p.p. it rose after the improvement of respiration, indicating that the pressor effect was secondary to the analeptic action.

CASE 3. A woman aged 66 years had a gastro-enterostomy which took about 1 hour. She received the following anaesthetic drugs: thiopentone 250 mg; d-tubocurarine 30 mg (in divided doses); nitrous oxide, oxygen and minimal ether. She was given atropine 1.2 mg and neostigmine 4 mg in divided doses. Although she responded to these, her respiration still appeared depressed; 2 ml of p.p.p. were injected and within 1 minute she had deeper respirations, opened her eyes and responded to questions.

Of the twenty-seven cases of depressed respiration, twenty-five showed definite improvement following the injection of p.p.p.

Two patients were apnoeic after operation; both had received muscle relaxants and respiration had been controlled. One patient had been given suxamethonium and halothane and, in the other, d-tubocurarine chloride and ether had been followed by atropine and neostigmine. It was thought that in both cases apnoea was due to a combination of central depression by the anaesthetic with an upset of the blood carbon dioxide resulting from controlled respiration. The injection of p.p.p. restored adequate respiratory depth and rate.

The drug was also given to a patient suffering from carbon dioxide narcosis and to one showing Cheyne-Stokes respiration.

CASE 4. Carbon dioxide narcosis developed in a woman of 78 years who underwent an operation for intestinal obstruction. The anaesthetic agents used were thiopentone, nitrous oxide, oxygen, cyclopropane, ether and d-tubocurarine. The anaesthetic had been given by another anaesthetist. She was seen by the author 3 hours later when she was obviously in extremis. An injection of p.p.p. had no effect and various other resuscitative measures were also of no avail. It may be that this patient's condition had reached an irreversible stage when p.p.p. was tried.

CASE 5. The patient who developed Cheyne-Stokes respiration was a man aged 70 years who had an amputation of leg under thiopentone, nitrous oxide, oxygen and halothane anaesthesia lasting 15 minutes. He was a very poor risk, having had a coronary thrombosis two months previously. He had marked arteriosclerosis, auricular fibrillation and was confused. After operation he developed typical Cheyne-Stokes respiration. This was unaffected by an injection of p.p.p. but responded to oxygen inhalation.

During the course of this investigation several similar cases were given nikethamide in order to compare the effects of the two drugs. Although no attempt at a controlled comparison was made it was clinically evident that their effects were closely similar. One patient with frequent and prolonged periods of apnoea following operation which showed little response to nikethamide responded well to p.p.p.

CASE 6. A man aged 53 years was anaesthetized with thiopentone, nitrous oxide, oxygen and halothane with a view to prostatectomy. He was a rather poor risk, having arteriosclerosis and an enlarged heart; his e.c.g. showed changes indicative of left ventricular strain.

For technical reasons the prostatectomy was abandoned and a suprapubic cystostomy was performed. He was anaesthetized for 45 minutes.

About 20 minutes after the anaesthetic had been started it was observed that the breathing was shallow and there was a tendency to cyanosis. The halothane was stopped but there was no improvement. The pulse was full and bounding and the patient's face was congested. The patient could only be kept

pink by giving 100 per cent oxygen intermittently and his respirations remained poor in depth and irregular.

At the end of the operation he had frequent and prolonged periods of apnoea and his lungs had to be inflated with oxygen. He was given nikethamide 2 ml intravenously. This abolished the periodic apnoea but the respiratory rate was still irregular and the depth somewhat shallow.

About 10 minutes later it was decided to inject p.p.p. At this stage he could not be roused and did not respond to painful stimuli. Following the injection of p.p.p. respirations became deeper and regular and within a minute he opened his eyes and responded to questions. An experienced nurse standing by considered his recovery most dramatic.

No ill effects were noticed following the use of p.p.p. in any of the forty cases in this series.

DISCUSSION

This series, which extended over a course of more than a year, was undertaken primarily as part of a study of problems connected with postoperative hypotension, and particularly of the sudden drop of blood pressure which sometimes occurs following the lowering of the legs after transurethral prostatectomy. The causes of this are somewhat obscure and may not be the same in all cases. It is regarded by some as a vasovagal phenomena for which atropine is sometimes given, but is more probably due to blood loss and pelvi-cardiac reflexes.

The results of the series reported here indicate that although p.p.p. undoubtedly possesses a pressor action it is not the treatment of choice in cases of this type, although in less severe cases, where the use of methoxamine is often followed by severe postoperative headache, it may be of some value. However, the analeptic effect of the drug is striking; it increases the depth of respiration and can change irregular respirations to regular. It appears also to lighten the depth of anaesthesia, probably as a secondary consequence of its analeptic action.

SUMMARY AND CONCLUSIONS

The postoperative use of phenyl-pyrrolidino-pentane in a series of forty patients is reported. The postoperative blood pressure was recorded in nine cases: in six there was a small rise and in three no change. In twenty-eight cases a marked analeptic action similar to that of nikethamide was noted. No untoward effects of the drug were observed.

It is concluded that phenyl-pyrrolidino-pentane is not the treatment of choice in the treatment of severe postoperative hypotension but that it is capable of markedly stimulating respiration, of producing an increase in the depth of respiratory movements, and of abolishing irregularities of breathing.

ACKNOWLEDGMENT

I wish to thank the Boehringer Ingelheim Division (Pfizer Ltd.) for making supplies of the drug available and for obtaining translations of the German literature.

REFERENCES

Kadatz, R., and Potsch, E. (1957). Pharmacology of 1-phenyl-2-pyrrolidino-pentane: a new analeptic. *Arzneimittel-Forsch.*, **7**, 6.

Kafer, K. (1957). A study of hypotension and the therapeutic value of phenylpyrrolidinopentane. *Münch. med. Wschr.*, **99**, 951.

Pabst, H. W. (1958). The actions of 1-phenyl-2-pyrrolidinopentane. *Arzneimittel-Forsch.*, **8**, 417.

Sniper, W. (1960). Postoperative postural hypotension. *Anaesthesia*, **15**, 33.

Brit. J. Anaesth. (1961), **33**, 417

A COMPOSITE SEMICLOSED ANAESTHETIC SYSTEM SUITABLE FOR CONTROLLED OR SPONTANEOUS RESPIRATION

BY

D. J. WATERS*

Department of Anaesthetics, Welsh National School of Medicine, Cardiff, Wales

FOR patients who are breathing spontaneously the Magill attachment or system A (Mapleson, 1954) is the most widely used semiclosed anaesthetic system. A theoretical analysis predicted that if the fresh-gas inflow were made at least equal to the patient's minute-volume ventilation, then rebreathing would be eliminated (Mapleson, 1954). A similar conclusion has been reached experimentally by various workers.

For patients whose respiration is manually controlled, however, a recent study (Waters and Mapleson, 1961) has shown that system D involves less rebreathing than system A. In the course of that investigation, an arrangement was devised which enabled the anaesthetist to change over easily from one to the other. This is now described in the belief that it may have some value in ordinary clinical anaesthesia when it is desired to avoid the use of soda lime.

* Present address: University College, Ibadan, Nigeria.

DESCRIPTION

Figure 1 illustrates the complete circuit. Two tubes run from the anaesthetic machine to the patient; one is a corrugated breathing tube and the other is a narrow-bore delivery tube. They lead to an expiratory valve mount (1). Both tubes take origin from a special device which plugs into the outlet of a Boyle's machine.

The tap (2) consists of two metal cylinders, one rotating inside the other. The inner cylinder (5) receives fresh gas from the Boyle apparatus but is permanently blocked off towards its other end. Gas escapes through an orifice in its wall. When the tap is in the "A" position this orifice is opposite another one in the outer cylinder. Gas passes out, and is led through a short metal tube (6) into the bag (4) and breathing tube. At the same time a prolongation of the inner cylinder closes off the pathway to the expiratory valve (3).

When the tap is in the "D" position the fresh

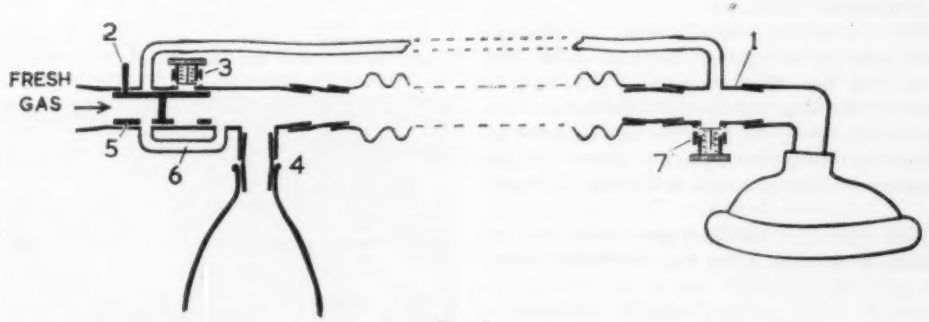


FIG. 1

1. Expiratory valve mount.
2. Control tap for A or D systems.
3. Expiratory valve for use with system D.
4. Reservoir bag.
5. Inner cylinder of tap.
6. Short metal tube.
7. Expiratory valve for use with system A.

N.B.—The figure shows the apparatus in the "A" position.

gas is directed along the narrow-bore tube instead of going into the bag. The expiratory valve (3) adjacent to the bag is now in action.

When system A is required the tap (2) is turned to the "A" position, and the valve (7) near the patient is brought into use. When system D is required, the valve (7) near the patient is closed, the tap (2) is turned to the "D" position, and the valve (3) near the bag operates; it needs only to be adjusted so that when the bag is squeezed, sufficient pressure can be built up in the system to inflate the patient's lungs.

DISADVANTAGES OF THE SYSTEM COMPARED WITH AN INFLATING VALVE

(1) Every time that a change is made from A to D, the valve near the patient must be manipulated. This may be inconvenient if the valve is covered by towels.

(2) Because system D is not entirely free of rebreathing, even when the fresh-gas flow equals the minute-volume ventilation, a larger ventilation is needed to maintain a satisfactory alveolar carbon dioxide level. This may lead to a somewhat higher intrathoracic pressure, with its undesirable side effects.

(3) The system, unlike most inflating valves, does demand some understanding on the part of the person using it.

ADVANTAGES OF THE SYSTEM OVER AN INFLATING VALVE

In spontaneous respiration.

When an inflating valve is used, the fresh-gas flow needs to be adjusted carefully. If the flow is too big the valve remains in the inflating position: the lungs are then held distended. If the flow is too small, the reservoir bag does not fill adequately during the expiratory phase: the bag empties while the patient is still trying to breathe in.

With system A the fresh-gas flow is far less critical. If the flow is too big, the excess escapes easily through the expiratory valve. If it is too small (less than the patient's minute-volume ventilation) the bag refills in expiration but does so partly with alveolar gas which is rebreathed during the next inspiration.

In controlled respiration.

When an inflating valve (such as the Ruben) is used, the bag cannot be left unattended for long when the patient is apnoeic, or the valve may be forced into the inflating position and be held there. The anaesthetist is thus tied to the bag. If rhythmic inflation must be stopped for any reason, then the supply of fresh gas must be turned off. With system D the bag can be safely left alone provided that the expiratory valve (3) is made slack.

All inflating valves direct the patient's expiration to the atmosphere and not back into the bag. Throughout the whole of the expiratory phase, therefore, the anaesthetist's hand is out of touch with the patient's airway and he may be unaware for a time that (for example) spontaneous respiration is returning. With system D the bag is always connected to the airway.

It may be added that when the device is used in the "D" position, and the bag is removed, then system E is produced (the T-piece system). System B can be produced if desired but it seems to offer no advantages.

Messrs. Medical and Industrial Equipment Ltd. have kindly agreed to manufacture the apparatus to order.

ACKNOWLEDGMENT

I am indebted to Mr. E. K. Hillard, L.I.B.S.T., Senior Technician to this Department, for advising on the design of the apparatus, and for constructing it.

REFERENCES

Mapleson, W. W. (1954). The elimination of rebreathing in various semi-closed anaesthetic systems. *Brit. J. Anaesth.*, **26**, 323.

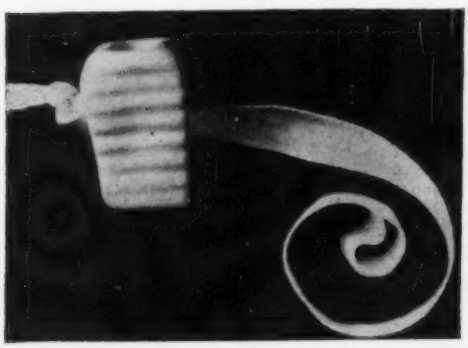
Waters, D. J., and Mapleson, W. W. (1961). Rebreathing during controlled respiration with various semiclosed anaesthetic systems. *Brit. J. Anaesth.*, **33**, 374.

CORRESPONDENCE

AN EDIBLE DENTAL PROP

Sir,—The first experience of anaesthesia is, for the majority of children, that accompanying a dental extraction. And if this experience is a terrifying one it will have an adverse effect on their reaction to anaesthesia for the rest of their life. On entering the dental surgery a small child is naturally apprehensive; there are many objects to be seen and he is asked to sit in a chair which is unlike any he has sat in before. The dental surgeon and the anaesthetist do their best to reassure him and to explain what is going to happen. Then to his surprise he is asked to open his mouth and bite on a prop. He is perhaps told to "bite on this piece of tin toffee". He bites, and on finding that it is not remotely like toffee, he spits it out. Attempts to replace it result in screams, which only too often end in the anaesthetist in desperation forcing the mask on to his face despite his struggles. Anaesthesia is eventually achieved but then a fresh struggle starts to insert a gag between his clenched teeth, often ending in trauma.

All this could have been avoided if the confidence of the child had not been destroyed by the lie about "tin toffee". It occurred to me that if a prop could be made to look—and taste—like a sweet, and at the same time efficiently hold the jaws apart without slipping, much would be gained. Taking the McKesson rubber prop as a model, attempts were made to reproduce it by pouring melted wine gums into a mould. But this proved too sticky and ordinary lozenge paste was substituted. This has a pleasant taste, does not fragment on pressure and can be produced as a perfect model of the original in any desired colour. A hole is bored through the middle to take a piece of tape to prevent accidental ingestion, as shown in the photograph.



The majority of children readily accept this prop and it is not easily dislodged during induction. The child is told that he will be given his sweet to take home with him after the extraction. After anaesthesia the prop is washed, the tape removed and it is handed to the child in the recovery room. It is remarkable how many crying children become quiet on receiving their "sweet". It may reasonably be argued by the dental profession that this will appear contradictory to their campaign to stop caries due to excessive sweet consumption. But the sweet might be used as a prize to reward the child for his co-operation with the dental surgeon.

MASSEY DAWKINS
London

CHLOROFORM AND HALOTHANE

Sir—It was refreshing to read the article by Drs. Dobkin, Harland and Fědoruk, "Chloroform and Halothane in a Precision System" (*Brit. J. Anaesth.*, **33**, 239). Their experimental work on dogs, the conclusions they draw and their general discussion of the subject are wholly admirable. In view of their remarks on the difficulty of comparing the two agents in a clinical study, the following brief account of an attempt at such a study, however imperfect, may be of interest:

Two years ago, a "Chlorotec" vaporizer was made available to me and I decided to anaesthetize patients in routine day-to-day operating lists, substituting chloroform given from a "Chorotec" inhaler for halothane given from a "Fluotec" inhaler in comparable strengths, but leaving the anaesthetic technique and administration otherwise unchanged. Fifty patients in all were thus anaesthetized; 8 for ear nose and throat surgery,

11 for general surgery, 18 for orthopaedic surgery, and 13 for major dental surgery. Premedication consisted of papaveretum 20 mg with hyoscine 0.4 mg, or morphine 10 mg with atropine 0.6 mg, or atropine 0.6 mg alone; the first combination was used for fit in-patients, the second for the less fit and those over 60 years of age, and the third for out-patients having minor orthopaedic operations. Anaesthesia was induced with thiopentone 100–400 mg as indicated and anaesthesia was maintained with 6 and 2 l./min respectively of nitrous oxide and oxygen, supplemented with chloroform. The amount of chloroform given varied with the needs of the patient; 2 per cent might be given for 1–2 minutes, followed by 1 per cent for 1–2 minutes, then ½ per cent thereafter. Only occasionally was it found necessary to increase the chloroform vapour strength to 1 per cent for 2–3 minutes during maintenance because of lightening of the level of anaesthesia. Twenty-four patients were intubated; 16 including all the major dental cases, nasally, and 8 orally. Suxamethonium chloride 30–40 mg was given when this was done. Three patients were artificially ventilated and laudexium was used as the relaxant for this purpose. Ventilation was by manual compression of a reservoir bag, using the Magill system which was employed in the whole series, and obtaining the necessary pressure by closing the Magill valve to the required degree. During artificial ventilation ½ per cent chloroform was used intermittently only for approximately half the total period of ventilation.

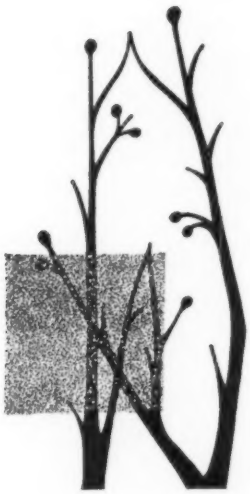
Among this series of patients were one aged 80 years and one aged 88 years with evidence of a recent pneumonia, both having operative treatment of a fractured femur; two diabetics; one with a history of coronary thrombosis; and one patient who was anaesthetized twice.

It would be unscientific to draw any firm conclusions from such a small series, but the clinical condition of these patients during and after anaesthesia suggested the following observations, which may be compared with the points made by Dobkin, Harland and Fedoruk in the article referred to above. (1) Chloroform and halothane are roughly equipotent in human beings. (2) Halothane will "settle" patients after a thiopentone induction slightly more quickly than chloroform. (3) Though reflexes, or coughing on extubation, are usually present at the end of operation whether chloroform or halothane is used as described above, complete recovery is a little more rapid after halothane. In a series of orthopaedic out-patients in which the drugs were used alternately, patients left the hospital in the same time, irrespective of which was used. (4) Apnoea was not seen with either drug as used in this technique, unless muscle relaxants had also been given. (5) Six out of 50 patients vomited postoperatively after chloroform; 2 after mastoidectomy and 1 after tonsillectomy. Two others brought up only a small quantity of mucus and the last, a healthy woman of 64, having previously had chloroform with no vomiting, vomited on the second occasion for 48 hours intermittently.

Duration of operations in the series was 15–90 minutes.

T. D. CULBERT
Manchester

Printed in Great Britain by John Sherratt & Son, Park Road, Altrincham



duncaine*

The new name for

Lignocaine and your guarantee

that it is from

DUNCAN FLOCKHART OF EDINBURGH

The Doctors' House

*A registered trade mark, the property of

DUNCAN, FLOCKHART & CO LTD EDINBURGH 11

388

BRITISH JOURNAL OF ANAESTHESIA

VOLUME XXXIII No. 8 *Published monthly* AUGUST 1961

Annual subscription (post free): Inland £3 15s.; Overseas £4 4s.; U.S. and South Americas $12.00

CONTENTS

PAGE

EDITORIAL 373

ORIGINAL

Rebreathing during controlled respiration with various semiclosed anaesthetic systems 374
By D. J. Waters, M.A., B.M., B.Ch., F.F.A.R.C.S., and W. W. Mapleson, Ph.D., A.Inst.P., Department of Anaesthetics, Welsh National School of Medicine, Cardiff, Wales.

CLINICAL

The effects of premedication with phenothiazine derivatives on the course of methohexitone anaesthesia 382
By John W. Dundee, M.D., Ph.D., F.F.A.R.C.S., and James Moore, M.B., F.F.A.R.C.S., Department of Anaesthetics, The Queen's University of Belfast, Belfast, Northern Ireland.

Postoperative amnesia 397
By W. Lambrechts, M.B., Ch.B.(Cape Town), D.A., and J. Parkhouse, M.A., M.D., F.F.A.R.C.S., D.A., Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford, England.

PAGE

Abnormal response to suxamethonium in polyarteritis nodosa 405
By M. W. Potts, F.F.A.R.C.S., and J. A. Thornton, F.F.A.R.C.S., Department of Anaesthetics, Guy's Hospital, London, S.E.1.

A method of anaesthesia for Caesarean section: evolution of a technique suitable for use in a country hospital ... 408
By C. A. G. Armstrong, M.B., D.A. (R.C.P.&S.I.), Mid-Ulster Hospital, Magherafelt, Co. Londonderry, Northern Ireland.

The analeptic action of phenyl-pyrrolidino-pentane 414
By W. Sniper, M.B., Ch.B., F.F.A.R.C.S., Stobhill General Hospital, Glasgow, Scotland.

APPARATUS

A composite semiclosed anaesthetic system suitable for controlled or spontaneous respiration 417
By D. J. Waters, M.A., B.M., B.Ch., F.F.A.R.C.S., Department of Anaesthetics, Welsh National School of Medicine, Cardiff, Wales.

BOOK REVIEW 407

CORRESPONDENCE 419

JOHN SHERRATT & SON *Publishers* **PARK ROAD ALTRINCHAM ENGLAND**